Product and Method

This application is a 371 of PCT/GB2003/005102, filed November 21, 2003, the disclosure of which is incorporated herein by reference.

A Sequence Listing on a single CD-ROM was filed with this application (file name: Q87920.ST25.txt). The Sequence Listing contains each of the polynucleotide and polypeptide sequences disclosed herein. The Sequence Listing is incorporated herein by reference.

The present invention relates to oligonucleotide probes, for use in assessing gene transcript levels in a cell, which may be used in analytical techniques, particularly diagnostic techniques. Conveniently the probes are provided in kit form. Different sets of probes may be used in techniques to prepare gene expression patterns and identify, diagnose or monitor different states, such as diseases, conditions or stages thereof. Also provided are methods of identifying suitable probes and their use in methods of the invention.

The identification of quick and easy methods of sample analysis for, for example, diagnostic applications, remains the goal of many researchers. End users seek methods which are cost effective, produce statistically significant results and which may be implemented routinely without the need for highly skilled individuals.

The analysis of gene expression within cells has been used to provide information on the state of those cells and importantly the state of the individual from which the cells are derived. The relative expression of various genes in a cell has been identified as reflecting a particular state within a body. For

example, cancer cells are known to exhibit altered expression of various proteins and the transcripts or the expressed proteins may therefore be used as markers of that disease state.

Thus biopsy tissue may be analysed for the presence of these markers and cells originating from the site of the disease may be identified in other tissues or fluids of the body by the presence of the markers.

Furthermore, products of the altered expression may be released into the blood stream and these products may be analysed. In addition cells which have contacted disease cells may be affected by their direct contact with those cells resulting in altered gene expression and their expression or products of expression may be

However, there are some limitations with these methods. For example, the use of specific tumour markers for identifying cancer suffers from a variety of defects, such as lack of specificity or sensitivity, association of the marker with disease states besides the specific type of cancer, and difficulty of detection in asymptomatic individuals.

similarly analysed.

In addition to the analysis of one or two marker transcripts or proteins, more recently, gene expression patterns have been analysed. Most of the work involving large-scale gene expression analysis with implications in disease diagnosis has involved clinical samples originating from diseased tissues or cells. For example, several recent publications, which demonstrate that gene expression data can be used to distinguish between similar cancer types, have used clinical samples from diseased tissues or cells (Alon et al. 1999, PNAS, 96, p6745-6750; Golub et al. 1999, Science, 286, p531-537; Alizadeh et al, 2000, Nature, 403, p503-511; Bittner et al., 2000, Nature, 406, p536-540).

However, these methods have relied on analysis of a

sample containing diseased cells or products of those cells or cells which have been contacted by disease cells. Analysis of such samples relies on knowledge of the presence of a disease and its location, which may be difficult in asymptomatic patients. Furthermore, samples can not always be taken from the disease site, e.g. in diseases of the brain.

In a finding of great significance, the present inventors identified the previously untapped potential of all cells within a body to provide information relating to the state of the organism from which the cells were derived. W098/49342 describes the analysis of the gene expression of cells distant from the site of disease, e.g. peripheral blood collected distant from a cancer site.

This finding is based on the premise that the different parts of an organism's body exist in dynamic interaction with each other. When a disease affects one part of the body, other parts of the body are also affected. The interaction results from a wide spectrum of biochemical signals that are released from the diseased area, affecting other areas in the body. Although, the nature of the biochemical and physiological changes induced by the released signals can vary in the different body parts, the changes can be measured at the level of gene expression and used for diagnostic purposes.

The physiological state of a cell in an organism is determined by the pattern with which genes are expressed in it. The pattern depends upon the internal and external biological stimuli to which said cell is exposed, and any change either in the extent or in the nature of these stimuli can lead to a change in the pattern with which the different genes are expressed in the cell. There is a growing understanding that by analysing the systemic changes in gene expression

patterns in cells in biological samples, it is possible to provide information on the type and nature of the biological stimuli that are acting on them. Thus, for example, by monitoring the expression of a large number of genes in cells in a test sample, it is possible to determine whether their genes are expressed with a pattern characteristic for a particular disease, condition or stage thereof. Measuring changes in gene activities in cells, e.g. from tissue or body fluids is therefore emerging as a powerful tool for disease diagnosis.

Such methods have various advantages. Often, obtaining clinical samples from certain areas in the body that is diseased can be difficult and may involve undesirable invasions in the body, for example biopsy is often used to obtain samples for cancer. In some cases, such as in Alzheimer's disease the diseased brain specimen can only be obtained post-mortem. Furthermore, the tissue specimens which are obtained are often heterogeneous and may contain a mixture of both diseased and non-diseased cells, making the analysis of generated gene expression data both complex and difficult.

It has been suggested that a pool of tumour tissues that appear to be pathogenetically homogeneous with respect to morphological appearances of the tumour may well be highly heterogeneous at the molecular level (Alizadeh, 2000, supra), and in fact might contain tumours representing essentially different diseases (Alizadeh, 2000, supra; Golub, 1999, supra). For the purpose of identifying a disease, condition, or a stage thereof, any method that does not require clinical samples to originate directly from diseased tissues or cells is highly desirable since clinical samples representing a homogeneous mixture of cell types can be obtained from an easily accessible region in the body.

We have now identified a set of probes of

surprising utility for identifying one or more diseases. Thus, we now describe probes and sets of probes derived from cells which are not disease cells and which have not contacted disease cells, which correspond to genes which exhibit altered expression in normal versus disease individuals, for use in methods of identifying, diagnosing or monitoring certain conditions, particularly diseases or stages thereof.

Thus the invention provides a set of oligonucleotide probes which correspond to genes in a cell whose expression is affected in a pattern characteristic of a particular disease, condition or stage thereof, wherein said genes are systemically affected by said disease, condition or stage thereof. Preferably said genes are metabolic or house-keeping genes and preferably are constitutively moderately or highly expressed. Preferably the genes are moderately or highly expressed in the cells of the sample but not in cells from disease cells or in cells having contacted such disease cells.

Such probes, particularly when isolated from cells distant to the site of disease, do not rely on the development of disease to clinically recognizable levels and allow detection of a disease or condition or stage thereof very early after the onset of said disease or condition, even years before other subjective or objective symptoms appear.

As used herein "systemically" affected genes refers to genes whose expression is affected in the body without direct contact with a disease cell or disease site and the cells under investigation are not disease cells.

"Contact" as referred to herein refers to cells coming into close proximity with one another such that the direct effect of one cell on the other may be observed, e.g. an immune response, wherein these

responses are not mediated by secondary molecules released from the first cell over a large distance to affect the second cell. Preferably contact refers to physical contact, or contact that is as close as is sterically possible, conveniently, cells which contact one another are found in the same unit volume, for example within 1cm³.

A "disease cell" is a cell manifesting phenotypic changes and is present at the disease site at some time during its life-span, e.g. a tumour cell at the tumour site or which has disseminated from the tumour, or a brain cell in the case of brain disorders such as Alzheimer's disease.

"Metabolic" or "house-keeping" genes refer to those genes responsible for expressing products involved in cell division and maintenance, e.g. non-immune function related genes.

"Moderately or highly" expressed genes refers to those present in resting cells in a copy number of more than 30--100 copies/cell (assuming an average $3\text{x}10^5$ mRNA molecules in a cell).

Specific probes having the above described properties are provided herein.

Thus in one aspect, the present invention provides a set of oligonucleotide probes, wherein said set comprises at least 10 oligonucleotides selected from:

an oligonucleotide as described in Table 1 or derived from a sequence described in Table 1, or an oligonucleotide with a complementary sequence, or a functionally equivalent oligonucleotide.

"Table 1" as referred to herein refers to Table 1a and/or Table 1b. Table 1b contains reference to additional clones and sequences as disclosed herein. Similarly Tables 2 and 4 comprise 2 parts, a and b.

The invention also provides one or more oligonucleotide probes, wherein each oligonucleotide

probe is selected from the oligonucleotides listed in Table 1, or derived from a sequence described in Table 1, or a complementary sequence thereof. The use of such probes in products and methods of the invention, form further aspects of the invention. As referred to herein an "oligonucleotide" is a nucleic acid molecule having at least 6 monomers in the polymeric structure, ie. nucleotides or modified forms thereof. The nucleic acid molecule may be DNA, RNA or PNA (peptide nucleic acid) or hybrids thereof or modified versions thereof, e.g. chemically modified forms, e.g. LNA (Locked Nucleic acid), by methylation or made up of modified or nonnatural bases during synthesis, providing they retain their ability to bind to complementary sequences. oligonucleotides are used in accordance with the invention to probe target sequences and are thus referred to herein also as oligonucleotide probes or simply as probes.

An "oligonucleotide derived from a sequence described in Table 1" (or any other table) refers to a part of a sequence disclosed in that Table (e.g. Table 1-4), which satisfies the requirements of the oligonucleotide probes as described herein, e.g. in length and function. Preferably said parts have the size described hereinafter.

Preferably the oligonucleotide probes forming said set are at least 15 bases in length to allow binding of target molecules. Especially preferably said oligonucleotide probes are from 20 to 200 bases in length, e.g. from 30 to 150 bases, preferably 50-100 bases in length.

As referred to herein the term "complementary sequences" refers to sequences with consecutive complementary bases (ie. T:A, G:C) and which complementary sequences are therefore able to bind to one another through their complementarity.

Reference to "10 oligonucleotides" refers to 10 different oligonucleotides. Whilst a Table 1 oligonucleotide, a Table 1 derived oligonucleotide and their functional equivalent are considered different oligonucleotides, complementary oligonucleotides are not considered different. Preferably however, the at least 10 oligonucleotides are 10 different Table 1 oligonucleotides (or Table 1 derived oligonucleotides or their functional equivalents). Thus said 10 different oligonucleotides are preferably able to bind to 10 different transcripts.

Preferably said oligonucleotides are as described in Table 1 or are derived from a sequence described in Table 1. Especially preferably said oligonucleotides are as described in Table 2 or Table 4 or are derived from a sequence described in either of those tables. Especially preferably the oligonucleotide (or the oligonucleotide derived therefrom) has a high occurrence as defined in Table 3, especially preferably >40%, e.g. >80 or >90, e.g. 100%.

A "set" as described refers to a collection of unique oligonucleotide probes (ie. having a distinct sequence) and preferably consists of less than 1000 oligonucleotide probes, especially less than 500 probes, e.g. preferably from 10 to 500, e.g. 10 to 100, 200 or 300, especially preferably 20 to 100, e.g. 30 to 100 probes. In some cases less than 10 probes may be used, e.g. from 2 to 9 probes, e.g. 5 to 9 probes.

It will be appreciated that increasing the number of probes will prevent the possibility of poor analysis, e.g. misdiagnosis by comparison to other diseases which could similarly alter the expression of the particular genes in question. Other oligonucleotide probes not described herein may also be present, particularly if they aid the ultimate use of the set of oligonucleotide probes. However, preferably said set consists only of

said Table 1 oligonucleotides, Table 1 derived oligonucleotides, complementary sequences or functionally equivalent oligonucleotides, or a sub-set thereof (e.g. of the size as described above), preferably a sub-set for which sequences are provided herein (see Table 1 and its footnote). Especially preferably said set consists only of said Table 1 oligonucleotides, Table 1 derived oligonucleotides, or complementary sequences thereof, or a sub-set thereof.

Multiple copies of each unique oligonucleotide probe, e.g. 10 or more copies, may be present in each set, but constitute only a single probe.

A set of oligonucleotide probes, which may preferably be immobilized on a solid support or have means for such immobilization, comprises the at least 10 oligonucleotide probes selected from those described hereinbefore. Especially preferably said probes are selected from those having high occurrence as described in Table 3 and as mentioned above. As mentioned above, these 10 probes must be unique and have different sequences. Having said this however, two separate probes may be used which recognize the same gene but reflect different splicing events. However oligonucleotide probes which are complementary to, and bind to distinct genes are preferred.

As described herein a "functionally equivalent" oligonucleotide to those described in Table 1 or derived therefrom refers to an oligonucleotide which is capable of identifying the same gene as an oligonucleotide of Table 1 or derived therefrom, ie. it can bind to the same mRNA molecule (or DNA) transcribed from a gene (target nucleic acid molecule) as the Table 1 oligonucleotide or the Table 1 derived oligonucleotide (or its complementary sequence). Preferably said functionally equivalent oligonucleotide is capable of recognizing, ie. binding to the same splicing product as

a Table 1 oligonucleotide or a Table 1 derived oligonucleotide. Preferably said mRNA molecule is the full length mRNA molecule which corresponds to the Table 1 oligonucleotide or the Table 1 derived oligonucleotide.

As referred to herein "capable of binding" or "binding" refers to the ability to hybridize under conditions described hereinafter.

Alternatively expressed, functionally equivalent oligonucleotides (or complementary sequences) have sequence identity or will hybridize, as described hereinafter, to a region of the target molecule to which molecule a Table 1 oligonucleotide or a Table 1 derived oligonucleotide or a complementary oligonucleotide binds. Preferably, functionally equivalent oligonucleotides (or their complementary sequences) hybridize to one of the mRNA sequences which corresponds to a Table 1 oligonucleotide or a Table 1 derived oligonucleotide under the conditions described hereinafter or has sequence identity to a part of one of the mRNA sequences which corresponds to a Table 1 oligonucleotide or a Table 1 derived oligonucleotide. A "part" in this context refers to a stretch of at least 5, e.g. at least 10 or 20 bases, such as from 5 to 100, e.g. 10 to 50 or 15 to 30 bases.

In a particularly preferred aspect, the functionally equivalent oligonucleotide binds to all or a part of the region of a target nucleic acid molecule (mRNA or cDNA) to which the Table 1 oligonucleotide or Table 1 derived oligonucleotide binds. A "target" nucleic acid molecule is the gene transcript or related product e.g. mRNA, or cDNA, or amplified product thereof. Said "region" of said target molecule to which said Table 1 oligonucleotide or Table 1 derived oligonucleotide binds is the stretch over which complementarity exists. At its largest this region is

the whole length of the Table 1 oligonucleotide or Table 1 derived oligonucleotide, but may be shorter if the entire Table 1 sequence or Table 1 derived oligonucleotide is not complementary to a region of the target sequence.

Preferably said part of said region of said target molecule is a stretch of at least 5, e.g. at least 10 or 20 bases, such as from 5 to 100, e.g. 10 to 50 or 15 to 30 bases. This may for example be achieved by said functionally equivalent oligonucleotide having several identical bases to the bases of the Table 1 oligonucleotide or the Table 1 derived oligonucleotide. These bases may be identical over consecutive stretches, e.g. in a part of the functionally equivalent oligonucleotide, or may be present non-consecutively, but provide sufficient complementarity to allow binding to the target sequence.

Thus in a preferred feature, said functionally equivalent oligonucleotide hybridizes under conditions of high stringency to a Table 1 oligonucleotide or a Table 1 derived oligonucleotide or the complementary sequence thereof. Alternatively expressed, said functionally equivalent oligonucleotide exhibits high sequence identity to all or part of a Table 1 oligonucleotide. Preferably said functionally equivalent oligonucleotide has at least 70% sequence identity, preferably at least 80%, e.g. at least 90, 95, 98 or 99%, to all of a Table 1 oligonucleotide or a part thereof. As used in this context, a "part" refers to a stretch of at least 5, e.g. at least 10 or 20 bases, such as from 5 to 100, e.g. 10 to 50 or 15 to 30 bases, in said Table 1 oligonucleotide. Especially preferably when sequence identity to only a part of said Table 1 oligonucleotide is present, the sequence identity is high, e.g. at least 80% as described above.

Functionally equivalent oligonucleotides which

satisfy the above stated functional requirements include those which are derived from the Table 1 oligonucleotides and also those which have been modified by single or multiple nucleotide base (or equivalent) substitution, addition and/or deletion, but which nonetheless retain functional activity, e.g. bind to the same target molecule as the Table 1 oligonucleotide or the Table 1 derived oligonucleotide from which they are further derived or modified. Preferably said modification is of from 1 to 50, e.g. from 10 to 30, preferably from 1 to 5 bases. Especially preferably only minor modifications are present, e.g. variations in less than 10 bases, e.g. less than 5 base changes.

Within the meaning of "addition" equivalents are included oligonucleotides containing additional sequences which are complementary to the consecutive stretch of bases on the target molecule to which the Table 1 oligonucleotide or the Table 1 derived oligonucleotide binds. Alternatively the addition may comprise a different, unrelated sequence, which may for example confer a further property, e.g. to provide a means for immobilization such as a linker to bind the oligonucleotide probe to a solid support.

Particularly preferred are naturally occurring equivalents such as biological variants, e.g. allelic, geographical or allotypic variants, e.g. oligonucleotides which correspond to a genetic variant, for example as present in a different species.

Functional equivalents include oligonucleotides with modified bases, e.g. using non-naturally occurring bases. Such derivatives may be prepared during synthesis or by post production modification.

"Hybridizing" sequences which bind under conditions of low stringency are those which bind under non-stringent conditions (for example, 6x SSC/50% formamide at room temperature) and remain bound when washed under

conditions of low stringency (2 X SSC, room temperature, more preferably 2 X SSC, 42° C). Hybridizing under high stringency refers to the above conditions in which washing is performed at 2 X SSC, 65° C (where SSC = 0.15M NaCl, 0.015M sodium citrate, pH 7.2).

"Sequence identity" as referred to herein refers to the value obtained when assessed using ClustalW (Thompson et al., 1994, Nucl. Acids Res., 22, p4673-4680) with the following parameters:
Pairwise alignment parameters - Method: accurate,
Matrix: IUB, Gap open penalty: 15.00, Gap extension
penalty: 6.66;
Multiple alignment parameters - Matrix: IUB, Gap open
penalty: 15.00, % identity for delay: 30, Negative
matrix: no, Gap extension penalty: 6.66, DNA transitions
weighting: 0.5.

Sequence identity at a particular base is intended to include identical bases which have simply been derivatized.

The invention also extends to polypeptides encoded by the mRNA sequence to which a Table 1 oligonucleotide or a Table 1 derived oligonucleotide binds. The invention further extends to antibodies which bind to any of said polypeptides.

As described above, conveniently said set of oligonucleotide probes may be immobilized on one or more solid supports. Single or preferably multiple copies of each unique probe are attached to said solid supports, e.g. 10 or more, e.g. at least 100 copies of each unique probe are present.

One or more unique oligonucleotide probes may be associated with separate solid supports which together form a set of probes immobilized on multiple solid support, e.g. one or more unique probes may be immobilized on multiple beads, membranes, filters, biochips etc. which together form a set of probes, which

together form modules of the kit described hereinafter. The solid support of the different modules are conveniently physically associated although the signals associated with each probe (generated as described hereinafter) must be separately determinable.

Alternatively, the probes may be immobilized on discrete portions of the same solid support, e.g. each unique oligonucleotide probe, e.g. in multiple copies, may be immobilized to a distinct and discrete portion or region of a single filter or membrane, e.g. to generate an array.

A combination of such techniques may also be used, e.g. several solid supports may be used which each immobilize several unique probes.

The expression "solid support" shall mean any solid material able to bind oligonucleotides by hydrophobic, ionic or covalent bridges.

"Immobilization" as used herein refers to reversible or irreversible association of the probes to said solid support by virtue of such binding. If reversible, the probes remain associated with the solid support for a time sufficient for methods of the invention to be carried out.

Numerous solid supports suitable as immobilizing moieties according to the invention, are well known in the art and widely described in the literature and generally speaking, the solid support may be any of the well-known supports or matrices which are currently widely used or proposed for immobilization, separation etc. in chemical or biochemical procedures. Such materials include, but are not limited to, any synthetic organic polymer such as polystyrene, polyvinylchloride, polyethylene; or nitrocellulose and cellulose acetate; or tosyl activated surfaces; or glass or nylon or any surface carrying a group suited for covalent coupling of nucleic acids. The immobilizing moieties may take the

form of particles, sheets, gels, filters, membranes, microfibre strips, tubes or plates, fibres or capillaries, made for example of a polymeric material e.g. agarose, cellulose, alginate, teflon, latex or polystyrene or magnetic beads. Solid supports allowing the presentation of an array, preferably in a single dimension are preferred, e.g. sheets, filters, membranes, plates or biochips.

Attachment of the nucleic acid molecules to the solid support may be performed directly or indirectly. For example if a filter is used, attachment may be performed by UV-induced crosslinking. Alternatively, attachment may be performed indirectly by the use of an attachment moiety carried on the oligonucleotide probes and/or solid support. Thus for example, a pair of affinity binding partners may be used, such as avidin, streptavidin or biotin, DNA or DNA binding protein (e.g. either the lac I repressor protein or the lac operator sequence to which it binds), antibodies (which may be mono- or polyclonal), antibody fragments or the epitopes or haptens of antibodies. In these cases, one partner of the binding pair is attached to (or is inherently part of) the solid support and the other partner is attached to (or is inherently part of) the nucleic acid molecules.

As used herein an "affinity binding pair" refers to two components which recognize and bind to one another specifically (ie. in preference to binding to other molecules). Such binding pairs when bound together form a complex.

Attachment of appropriate functional groups to the solid support may be performed by methods well known in the art, which include for example, attachment through hydroxyl, carboxyl, aldehyde or amino groups which may be provided by treating the solid support to provide suitable surface coatings. Solid supports presenting

appropriate moieties for attachment of the binding partner may be produced by routine methods known in the art.

Attachment of appropriate functional groups to the oligonucleotide probes of the invention may be performed by ligation or introduced during synthesis or amplification, for example using primers carrying an appropriate moiety, such as biotin or a particular sequence for capture.

Conveniently, the set of probes described hereinbefore is provided in kit form.

Thus viewed from a further aspect the present invention provides a kit comprising a set of oligonucleotide probes as described hereinbefore immobilized on one or more solid supports.

Preferably, said probes are immobilized on a single solid support and each unique probe is attached to a different region of said solid support. However, when attached to multiple solid supports, said multiple solid supports form the modules which make up the kit. Especially preferably said solid support is a sheet, filter, membrane, plate or biochip.

Optionally the kit may also contain information relating to the signals generated by normal or diseased samples (as discussed in more detail hereinafter in relation to the use of the kits), standardizing materials, e.g. mRNA or cDNA from normal and/or diseased samples for comparative purposes, labels for incorporation into cDNA, adapters for introducing nucleic acid sequences for amplification purposes, primers for amplification and/or appropriate enzymes, buffers and solutions. Optionally said kit may also contain a package insert describing how the method of the invention should be performed, optionally providing standard graphs, data or software for interpretation of results obtained when performing the invention.

The use of such kits to prepare a standard diagnostic gene transcript pattern as described hereinafter forms a further aspect of the invention.

The set of probes as described herein have various uses. Principally however they are used to assess the gene expression state of a test cell to provide information relating to the organism from which said cell is derived. Thus the probes are useful in diagnosing, identifying or monitoring a disease or condition or stage thereof in an organism.

Thus in a further aspect the invention provides the use of a set of oligonucleotide probes or a kit as described hereinbefore to determine the gene expression pattern of a cell which pattern reflects the level of gene expression of genes to which said oligonucleotide probes bind, comprising at least the steps of:

- a) isolating mRNA from said cell, which may optionally be reverse transcribed to cDNA;
- b) hybridizing the mRNA or cDNA of step (a) to a set of oligonucleotide probes or a kit as defined herein; and
- c) assessing the amount of mRNA or cDNA hybridizing to each of said probes to produce said pattern.

The mRNA and cDNA as referred to in this method, and the methods hereinafter, encompass derivatives or copies of said molecules, e.g. copies of such molecules such as those produced by amplification or the preparation of complementary strands, but which retain the identity of the mRNA sequence, ie. would hybridize to the direct transcript (or its complementary sequence) by virtue of precise complementarity, or sequence identity, over at least a region of said molecule. It will be appreciated that complementarity will not exist over the entire region where techniques have been used which may truncate the transcript or introduce new sequences, e.g. by primer amplification. For

convenience, said mRNA or cDNA is preferably amplified prior to step b). As with the oligonucleotides described herein said molecules may be modified, e.g. by using non-natural bases during synthesis providing complementarity remains. Such molecules may also carry additional moieties such as signalling or immobilizing means.

The various steps involved in the method of preparing such a pattern are described in more detail hereinafter.

As used herein "gene expression" refers to transcription of a particular gene to produce a specific mRNA product (ie. a particular splicing product). The level of gene expression may be determined by assessing the level of transcribed mRNA molecules or cDNA molecules reverse transcribed from the mRNA molecules or products derived from those molecules, e.g. by amplification.

The "pattern" created by this technique refers to information which, for example, may be represented in tabular or graphical form and conveys information about the signal associated with two or more oligonucleotides. Preferably said pattern is expressed as an array of numbers relating to the expression level associated with each probe.

Preferably, said pattern is established using the following linear model:

y = Xb + f Equation 1 wherein, X is the matrix of gene expression data and y is the response variable, b is the regression coefficient vector and f the estimated residual vector. Although many different methods can be used to establish the relationship provided in equation 1, especially preferably the partial Least Squares Regression (PLSR) method is used for establishing the relationship in equation 1.

The probes are thus used to generate a pattern which reflects the gene expression of a cell at the time of its isolation. The pattern of expression is characteristic of the circumstances under which that cells finds itself and depends on the influences to which the cell has been exposed. Thus, a characteristic gene transcript pattern standard or fingerprint (standard probe pattern) for cells from an individual with a particular disease or condition may be prepared and used for comparison to transcript patterns of test cells. This has clear applications in diagnosing, monitoring or identifying whether an organism is suffering from a particular disease, condition or stage thereof.

The standard pattern is prepared by determining the extent of binding of total mRNA (or cDNA or related product), from cells from a sample of one or more organisms with the disease or condition or stage thereof, to the probes. This reflects the level of transcripts which are present which correspond to each unique probe. The amount of nucleic acid material which binds to the different probes is assessed and this information together forms the gene transcript pattern standard of that disease or condition or stage thereof. Each such standard pattern is characteristic of the disease, condition or stage thereof.

In a further aspect therefore, the present invention provides a method of preparing a standard gene transcript pattern characteristic of a disease or condition or stage thereof in an organism comprising at least the steps of:

- a) isolating mRNA from the cells of a sample of one or more organisms having the disease or condition or stage thereof, which may optionally be reverse transcribed to cDNA;
 - b) hybridizing the mRNA or cDNA of step (a) to a

set of oligonucleotides or a kit as described hereinbefore specific for said disease or condition or stage thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation; and

c) assessing the amount of mRNA or cDNA hybridizing to each of said probes to produce a characteristic pattern reflecting the level of gene expression of genes to which said oligonucleotides bind, in the sample with the disease, condition or stage thereof.

For convenience, said oligonucleotides are preferably immobilized on one or more solid supports.

The standard pattern for a great number of diseases or conditions and different stages thereof using particular probes may be accumulated in databases and be made available to laboratories on request.

"Disease" samples and organisms as referred to herein refer to organisms (or samples from the same) with an underlying pathological disturbance relative to a normal organism (or sample), in a symptomatic or asymptomatic organism, which may result, for example, from infection or an acquired or congenital genetic imperfection. Such organisms are known to have, or which exhibit, the disease or condition or stage thereof under study.

A "condition" refers to a state of the mind or body of an organism which has not occurred through disease, e.g. the presence of an agent in the body such as a toxin, drug or pollutant, or pregnancy.

"Stages" thereof refer to different stages of the disease or condition which may or may not exhibit particular physiological or metabolic changes, but do exhibit changes at the genetic level which may be detected as altered gene expression. It will be appreciated that during the course of a disease or condition the expression of different transcripts may

vary. Thus at different stages, altered expression may not be exhibited for particular transcripts compared to "normal" samples. However, combining information from several transcripts which exhibit altered expression at one or more stages through the course of the disease or condition can be used to provide a characteristic pattern which is indicative of a particular stage of the disease or condition. Thus for example different stages in cancer, e.g. pre-stage I, stage I, stage II, II or IV can be identified.

"Normal" as used herein refers to organisms or samples which are used for comparative purposes. Preferably, these are "normal" in the sense that they do not exhibit any indication of, or are not believed to have, any disease or condition that would affect gene expression, particularly in respect of the disease for which they are to be used as the normal standard. However, it will be appreciated that different stages of a disease or condition may be compared and in such cases, the "normal" sample may correspond to the earlier stage of the disease or condition.

As used herein a "sample" refers to any material obtained from the organism, e.g. human or non-human animal under investigation which contains cells and includes, tissues, body fluid or body waste or in the case of prokaryotic organisms, the organism itself. "Body fluids" include blood, saliva, spinal fluid, semen, lymph. "Body waste" includes urine, expectorated matter (pulmonary patients), faeces etc. "Tissue samples" include tissue obtained by biopsy, by surgical interventions or by other means e.g. placenta. Preferably however, the samples which are examined are from areas of the body not apparently affected by the disease or condition. The cells in such samples are not disease cells, e.g. cancer cells, have not been in contact with such disease cells and do not originate

from the site of the disease or condition. The "site of disease" is considered to be that area of the body which manifests the disease in a way which may be objectively determined, e.g. a tumour or area of inflammation. Thus for example peripheral blood may be used for the diagnosis of non-haematopoietic cancers, and the blood does not require the presence of malignant or disseminated cells from the cancer in the blood. Similarly in diseases of the brain, in which no diseased cells are found in the blood due to the blood:brain barrier, peripheral blood may still be used in the methods of the invention.

It will however be appreciated that the method of preparing the standard transcription pattern and other methods of the invention are also applicable for use on living parts of eukaryotic organisms such as cell lines and organ cultures and explants. As used herein. reference to "corresponding" sample etc. refers to cells preferably from the same tissue, body fluid or body waste, but also includes cells from tissue, body fluid or body waste which are sufficiently similar for the purposes of preparing the standard or test pattern. When used in reference to genes "corresponding" to the probes, this refers to genes which are related by sequence (which may be complementary) to the probes although the probes may reflect different splicing products of expression.

"Assessing" as used herein refers to both quantitative and qualitative assessment which may be determined in absolute or relative terms.

The invention may be put into practice as follows.

To prepare a standard transcript pattern for a particular disease, condition or stage thereof, sample mRNA is extracted from the cells of tissues, body fluid or body waste according to known techniques (see for

example Sambrook et. al. (1989), Molecular Cloning: A laboratory manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.) from a diseased individual or organism.

Owing to the difficulties in working with RNA, the RNA is preferably reverse transcribed at this stage to form first strand cDNA. Cloning of the cDNA or selection from, or using, a cDNA library is not however necessary in this or other methods of the invention. Preferably, the complementary strands of the first strand cDNAs are synthesized, ie. second strand cDNAs, but this will depend on which relative strands are present in the oligonucleotide probes. The RNA may however alternatively be used directly without reverse transcription and may be labelled if so required.

Preferably the cDNA strands are amplified by known amplification techniques such as the polymerase chain reaction (PCR) by the use of appropriate primers. Alternatively, the cDNA strands may be cloned with a vector, used to transform a bacteria such as E. coli which may then be grown to multiply the nucleic acid molecules. When the sequence of the cDNAs are not known, primers may be directed to regions of the nucleic acid molecules which have been introduced. Thus for example, adapters may be ligated to the cDNA molecules and primers directed to these portions for amplification of the cDNA molecules. Alternatively, in the case of eukaryotic samples, advantage may be taken of the polyA tail and cap of the RNA to prepare appropriate primers.

To produce the standard diagnostic gene transcript pattern or fingerprint for a particular disease or condition or stage thereof, the above described oligonucleotide probes are used to probe mRNA or cDNA of the diseased sample to produce a signal for hybridization to each particular oligonucleotide probe species, ie. each unique probe. A standard control gene

transcript pattern may also be prepared if desired using mRNA or cDNA from a normal sample. Thus, mRNA or cDNA is brought into contact with the oligonucleotide probe under appropriate conditions to allow hybridization.

When multiple samples are probed, this may be performed consecutively using the same probes, e.g. on one or more solid supports, ie. on probe kit modules, or by simultaneously hybridizing to corresponding probes, e.g. the modules of a corresponding probe kit.

To identify when hybridization occurs and obtain an indication of the number of transcripts/cDNA molecules which become bound to the oligonucleotide probes, it is necessary to identify a signal produced when the transcripts (or related molecules) hybridize (e.g. by detection of double stranded nucleic acid molecules or detection of the number of molecules which become bound, after removing unbound molecules, e.g. by washing).

In order to achieve a signal, either or both components which hybridize (ie. the probe and the transcript) carry or form a signalling means or a part thereof. This "signalling means" is any moiety capable of direct or indirect detection by the generation or presence of a signal. The signal may be any detectable physical characteristic such as conferred by radiation emission, scattering or absorption properties, magnetic properties, or other physical properties such as charge, size or binding properties of existing molecules (e.g. labels) or molecules which may be generated (e.g. gas emission etc.). Techniques are preferred which allow signal amplification, e.g. which produce multiple signal events from a single active binding site, e.g. by the catalytic action of enzymes to produce multiple detectable products.

Conveniently the signalling means may be a label which itself provides a detectable signal. Conveniently this may be achieved by the use of a radioactive or

other label which may be incorporated during cDNA production, the preparation of complementary cDNA strands, during amplification of the target mRNA/cDNA or added directly to target nucleic acid molecules.

Appropriate labels are those which directly or indirectly allow detection or measurement of the presence of the transcripts/cDNA. Such labels include for example radiolabels, chemical labels, for example chromophores or fluorophores (e.g. dyes such as fluorescein and rhodamine), or reagents of high electron density such as ferritin, haemocyanin or colloidal gold. Alternatively, the label may be an enzyme, for example peroxidase or alkaline phosphatase, wherein the presence of the enzyme is visualized by its interaction with a suitable entity, for example a substrate. The label may also form part of a signalling pair wherein the other member of the pair is found on, or in close proximity to, the oligonucleotide probe to which the transcript/cDNA binds, for example, a fluorescent compound and a quench fluorescent substrate may be used. A label may also be provided on a different entity, such as an antibody, which recognizes a peptide moiety attached to the transcripts/cDNA, for example attached to a base used during synthesis or amplification.

A signal may be achieved by the introduction of a label before, during or after the hybridization step. Alternatively, the presence of hybridizing transcripts may be identified by other physical properties, such as their absorbance, and in which case the signalling means is the complex itself.

The amount of signal associated with each oligonucleotide probe is then assessed. The assessment may be quantitative or qualitative and may be based on binding of a single transcript species (or related cDNA or other products) to each probe, or binding of multiple transcript species to multiple copies of each unique

probe. It will be appreciated that quantitative results will provide further information for the transcript fingerprint of the disease which is compiled. This data may be expressed as absolute values (in the case of macroarrays) or may be determined relative to a particular standard or reference e.g. a normal control sample.

Furthermore it will be appreciated that the standard diagnostic gene pattern transcript may be prepared using one or more disease samples (and normal samples if used) to perform the hybridization step to obtain patterns not biased towards a particular individual's variations in gene expression.

The use of the probes to prepare standard patterns and the standard diagnostic gene transcript patterns thus produced for the purpose of identification or diagnosis or monitoring of a particular disease or condition or stage thereof in a particular organism forms a further aspect of the invention.

Once a standard diagnostic fingerprint or pattern has been determined for a particular disease or condition using the selected oligonucleotide probes, this information can be used to identify the presence, absence or extent or stage of that disease or condition in a different test organism or individual.

To examine the gene expression pattern of a test sample, a test sample of tissue, body fluid or body waste containing cells, corresponding to the sample used for the preparation of the standard pattern, is obtained from a patient or the organism to be studied. A test gene transcript pattern is then prepared as described hereinbefore as for the standard pattern.

In a further aspect therefore, the present invention provides a method of preparing a test gene transcript pattern comprising at least the steps of:

a) isolating mRNA from the cells of a sample of

said test organism, which may optionally be reverse transcribed to cDNA;

- b) hybridizing the mRNA or cDNA of step (a) to a set of oligonucleotides or a kit as described hereinbefore specific for a disease or condition or stage thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation; and
- c) assessing the amount of mRNA or cDNA hybridizing to each of said probes to produce said pattern reflecting the level of gene expression of genes to which said oligonucleotides bind, in said test sample.

This test pattern may then be compared to one or more standard patterns to assess whether the sample contains cells having the disease, condition or stage thereof.

Thus viewed from a further aspect the present invention provides a method of diagnosing or identifying or monitoring a disease or condition or stage thereof in an organism, comprising the steps of:

- a) isolating mRNA from the cells of a sample of said organism, which may optionally be reverse transcribed to cDNA;
- b) hybridizing the mRNA or cDNA of step (a) to a set of oligonucleotides or a kit as described hereinbefore specific for said disease or condition or stage thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation;
- c) assessing the amount of mRNA or cDNA hybridizing to each of said probes to produce a characteristic pattern reflecting the level of gene expression of genes to which said oligonucleotides bind, in said sample; and
- d) comparing said pattern to a standard diagnostic pattern prepared according to the

method of the invention using a sample from an organism corresponding to the organism and sample under investigation to determine the presence of said disease or condition or a stage thereof in the organism under investigation.

The method up to and including step c) is the preparation of a test pattern as described above.

As referred to herein, "diagnosis" refers to determination of the presence or existence of a disease or condition or stage thereof in an organism.

"Monitoring" refers to establishing the extent of a disease or condition, particularly when an individual is known to be suffering from a disease or condition, for example to monitor the effects of treatment or the development of a disease or condition, e.g. to determine the suitability of a treatment or provide a prognosis.

The presence of the disease or condition or stage thereof may be determined by determining the degree of correlation between the standard and test samples' patterns. This necessarily takes into account the range of values which are obtained for normal and diseased samples. Although this can be established by obtaining standard deviations for several representative samples binding to the probes to develop the standard, it will be appreciated that single samples may be sufficient to generate the standard pattern to identify a disease if the test sample exhibits close enough correlation to that standard. Conveniently, the presence, absence, or extent of a disease or condition or stage thereof in a test sample can be predicted by inserting the data relating to the expression level of informative probes in test sample into the standard diagnostic probe pattern established according to equation 1.

Data generated using the above mentioned methods may be analysed using various techniques from the most

basic visual representation (e.g. relating to intensity) to more complex data manipulation to identify underlying patterns which reflect the interrelationship of the level of expression of each gene to which the various probes bind, which may be quantified and expressed mathematically. Conveniently, the raw data thus generated may be manipulated by the data processing and statistical methods described hereinafter, particularly normalizing and standardizing the data and fitting the data to a classification model to determine whether said test data reflects the pattern of a particular disease, condition or stage thereof.

The methods described herein may be used to identify, monitor or diagnose a disease, condition or ailment or its stage or progression, for which the oligonucleotide probes are informative. "Informative" probes as described herein, are those which reflect genes which have altered expression in the diseases or conditions in question, or particular stages thereof. Probes of the invention may not be sufficiently informative for diagnostic purposes when used alone, but are informative when used as one of several probes to provide a characteristic pattern, e.g. in a set as described hereinbefore.

Preferably said probes correspond to genes which are systemically affected by said disease, condition or stage thereof. Especially preferably said genes, from which transcripts are derived which bind to probes of the invention, are metabolic or house-keeping genes and preferably are moderately or highly expressed. The advantage of using probes directed to moderately or highly expressed genes is that smaller clinical samples are required for generating the necessary gene expression data set, e.g. less than 1ml blood samples.

Furthermore, it has been found that such genes which are already being actively transcribed tend to be

more prone to being influenced, in a positive or negative way, by new stimuli. In addition, since transcripts are already being produced at levels which are generally detectable, small changes in those levels are readily detectable as for example, a certain detectable threshold does not need to be reached.

In preferred methods of the invention, the set of probes of the invention are informative for a variety of different diseases, conditions or stages thereof. sub-set of the probes disclosed herein may be used for diagnosis, identification or monitoring a particular disease, condition or stage thereof. Thus the probes may be used to diagnose or identify or monitor any condition, ailment, disease or reaction that leads to the relative increase or decrease in the activity of informative genes of any or all eukaryotic or prokaryotic organisms regardless of whether these changes have been caused by the influence of bacteria, virus, prions, parasites, fungi, radiation, natural or artificial toxins, drugs or allergens, including mental conditions due to stress, neurosis, psychosis or deteriorations due to the ageing of the organism, and conditions or diseases of unknown cause, providing a sub-set of the probes as described herein are informative for said disease or condition or stage thereof.

Such diseases include those which result in metabolic or physiological changes, such as fever-associated diseases such as influenza or malaria. Other diseases which may be detected include for example yellow fever, sexually transmitted diseases such as gonorrhea, fibromyalgia, candida-related complex, cancer (for example of the stomach, lung, breast, prostate gland, bowel, skin, colon, ovary etc), Alzheimer's disease, disease caused by retroviruses such as HIV, senile dementia, multiple sclerosis and Creutzfeldt-

Jakob disease to mention a few.

The invention may also be used to identify patients with psychiatric or psychosomatic diseases such as schizophrenia and eating disorders. Of particular importance is the use of this method to detect diseases, conditions, or stages thereof, which are not readily detectable by known diagnostic methods, such as HIV which is generally not detectable using known techniques 1 to 4 months following infection. Conditions which may be identified include for example drug abuse, such as the use of narcotics, alcohol, steroids or performance enhancing drugs.

Preferably said disease to be identified or monitored is a cancer or a degenerative brain disorder (such as Alzheimer's or Parkinson's disease).

In particular, a set of oligonucleotide probes, wherein said set comprises at least 10 oligonucleotides selected from:

an oligonucleotide as described in Table 4 or an oligonucleotide derived therefrom or an oligonucleotide with a complementary sequence, or a functionally equivalent oligonucleotide,

may be used for diagnosis or identification or monitoring the progression of Alzheimer's disease. Similarly Table 2 probes and Table 2 derived probes and their functional equivalents may be used to diagnose, identify or monitor the progression of breast cancer. Especially preferably the probes used for breast cancer analysis are selected based on their occurrence as set forth in Table 3 and as described hereinbefore.

The diagnostic method may be used alone as an alternative to other diagnostic techniques or in addition to such techniques. For example, methods of the invention may be used as an alternative or additive diagnostic measure to diagnosis using imaging techniques such as Magnetic Resonance Imagine (MRI), ultrasound

imaging, nuclear imaging or X-ray imaging, for example in the identification and/or diagnosis of tumours.

The methods of the invention may be performed on cells from prokaryotic or eukaryotic organisms which may be any eukaryotic organisms such as human beings, other mammals and animals, birds, insects, fish and plants, and any prokaryotic organism such as a bacteria.

Preferred non-human animals on which the methods of the invention may be conducted include, but are not limited to mammals, particularly primates, domestic animals, livestock and laboratory animals. Thus preferred animals for diagnosis include mice, rats, guinea pigs, cats, dogs, pigs, cows, goats, sheep, horses. Particularly preferably the disease state or condition of humans is diagnosed, identified or monitored.

As described above, the sample under study may be any convenient sample which may be obtained from an organism. Preferably however, as mentioned above, the sample is obtained from a site distant to the site of disease and the cells in such samples are not disease cells, have not been in contact with such cells and do not originate from the site of the disease or condition.

In such cases, although preferably absent, the sample may contain cells which do not fulfil these criteria. However, since the probes of the invention are concerned with transcripts whose expression is altered in cells which do satisfy these criteria, the probes are specifically directed to detecting changes in transcript levels in those cells even if in the presence of other, background cells.

It has been found that the cells from such samples show significant and informative variations in the gene expression of a large number of genes. Thus, the same probe (or several probes) may be found to be informative in determinations regarding two or more diseases,

conditions or stages thereof by virtue of the particular level of transcripts binding to that probe or the interrelationship of the extent of binding to that probe relative to other probes. As a consequence, it is possible to use a relatively small number of probes for screening for multiple disorders or diseases. This has consequences with regard to the selection of probes, discussed in relation to random identification of probes hereinafter, but also for the use of a single set of probes for more than one diagnosis. Table 9 which represents preferred probes of the invention discloses probes which are informative for both Alzheimer's and breast cancer.

Thus, the present invention also provides sets of probes for diagnosing, identifying or monitoring two or more diseases, conditions or stages thereof, wherein at least one of said probes is suitable for said diagnosing, identifying or monitoring at least two of said diseases, conditions or stages thereof, and kits and methods of using the same. Preferably at least 5 probes, e.g. from 5 to 15 probes, are used in at least two diagnoses.

Thus, in a further preferred aspect, the present invention provides a method of diagnosis or identification or monitoring as described hereinbefore for the diagnosis, identification or monitoring of two or more diseases, conditions or stages thereof in an organism, wherein said test pattern produced in step c) of the diagnostic method is compared in step d) to at least two standard diagnostic patterns prepared as described previously, wherein each standard diagnostic pattern is a pattern generated for a different disease or condition or stage thereof.

Whilst in a preferred aspect the methods of assessment concern the development of a gene transcript pattern from a test sample and comparison of the same to

a standard pattern, the elevation or depression of expression of certain markers may also be examined by examining the products of expression and the level of those products. Thus a standard pattern in relation to the expressed product may be generated.

In such methods the levels of expression of a set of polypeptides encoded by the gene to which an oligonucleotide of Table 1 or a Table 1 derived oligonucleotide, binds, are analysed.

Various diagnostic methods may be used to assess the amount of polypeptides (or fragments thereof) which are present. The presence or concentration of polypeptides may be examined, for example by the use of a binding partner to said polypeptide (e.g. an antibody), which may be immobilized, to separate said polypeptide from the sample and the amount of polypeptide may then be determined.

"Fragments" of the polypeptides refers to a domain or region of said polypeptide, e.g. an antigenic fragment, which is recognizable as being derived from said polypeptide to allow binding of a specific binding partner. Preferably such a fragment comprises a significant portion of said polypeptide and corresponds to a product of normal post-synthesis processing. Thus in a further aspect the present invention provides a method of preparing a standard gene transcript pattern characteristic of a disease or condition or stage thereof in an organism comprising at least the steps of:

- a) releasing target polypeptides from a sample of one or more organisms having the disease or condition or stage thereof;
- b) contacting said target polypeptides with one or more binding partners, wherein each binding partner is specific to a marker polypeptide (or a fragment thereof) encoded by the gene to which an oligonucleotide of Table 1 (or derived from a sequence described in Table 1)

binds, to allow binding of said binding partners to said target polypeptides, wherein said marker polypeptides are specific for said disease or condition thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation; and

c) assessing the target polypeptide binding to said binding partners to produce a characteristic pattern reflecting the level of gene expression of genes which express said marker polypeptides, in the sample with the disease, condition or stage thereof.

As used herein "target polypeptides" refer to those polypeptides present in a sample which are to be detected and "marker polypeptides" are polypeptides which are encoded by the genes to which Table 1 oligonucleotides or Table 1 derived oligonucleotides bind. The target and marker polypeptides are identical or at least have areas of high similarity, e.g. epitopic regions to allow recognition and binding of the binding partner.

"Release" of the target polypeptides refers to appropriate treatment of a sample to provide the polypeptides in a form accessible for binding of the binding partners, e.g. by lysis of cells where these are present. The samples used in this case need not necessarily comprise cells as the target polypeptides may be released from cells into the surrounding tissue or fluid, and this tissue or fluid may be analysed, e.g. urine or blood. Preferably however the preferred samples as described herein are used. "Binding partners" comprise the separate entities which together make an affinity binding pair as described above, wherein one partner of the binding pair is the target or marker polypeptide and the other partner binds specifically to that polypeptide, e.g. an antibody.

Various arrangements may be envisaged for detecting the amount of binding pairs which form. In its simplest

form, a sandwich type assay e.g. an immunoassay such as an ELISA, may be used in which an antibody specific to the polypeptide and carrying a label (as described elsewhere herein) may be bound to the binding pair (e.g. the first antibody:polypeptide pair) and the amount of label detected.

Other methods as described herein may be similarly modified for analysis of the protein product of expression rather than the gene transcript and related nucleic acid molecules.

Thus a further aspect of the invention provides a method of preparing a test gene transcript pattern comprising at least the steps of:

- a) releasing target polypeptides from a sample of said test organism;
- b) contacting said target polypeptides with one or more binding partners, wherein each binding partner is specific to a marker polypeptide (or a fragment thereof) encoded by the gene to which an oligonucleotide of Table 1 (or derived from a sequence described in Table 1) binds, to allow binding of said binding partners to said target polypeptides, wherein said marker polypeptides are specific for said disease or condition thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation; and
- c) assessing the target polypeptide binding to said binding partners to produce a characteristic pattern reflecting the level of gene expression of genes which express said marker polypeptides, in said test sample.

A yet further aspect of the invention provides a method of diagnosing or identifying or monitoring a disease or condition or stage thereof in an organism comprising the steps of:

- a) releasing target polypeptides from a sample of said organism;
 - b) contacting said target polypeptides with one or

more binding partners, wherein each binding partner is specific to a marker polypeptide (or a fragment thereof) encoded by the gene to which an oligonucleotide of Table 1 (or derived from a sequence described in Table 1) binds, to allow binding of said binding partners to said target polypeptides, wherein said marker polypeptides are specific for said disease or condition thereof in an organism and sample thereof corresponding to the organism and sample thereof under investigation; and

- c) assessing the target polypeptide binding to said binding partners to produce a characteristic pattern reflecting the level of gene expression of genes which express said marker polypeptides in said sample; and
- d) comparing said pattern to a standard diagnostic pattern prepared as described hereinbefore using a sample from an organism corresponding to the organism and sample under investigation to determine the degree of correlation indicative of the presence of said disease or condition or a stage thereof in the organism under investigation.

The methods of generating standard and test patterns and diagnostic techniques rely on the use of informative oligonucleotide probes to generate the gene expression data. In some cases it will be necessary to select these informative probes for a particular method, e.g. to diagnose a particular disease, from a selection of available probes, e.g. the probes described hereinbefore (the Table 1 oligonucleotides, the Table 1 derived oligonucleotides, their complementary sequences and functionally equivalent oligonucleotides). The following methodology describes a convenient method for identifying such informative probes, or more particularly how to select a suitable sub-set of probes from the probes described herein.

Probes for the analysis of a particular disease or condition or stage thereof, may be identified in a

number of ways known in the prior art, including by differential expression or by library subtraction (see for example WO98/49342). As described hereinafter, in view of the high information content of most transcripts, as a starting point one may also simply analyse a random sub-set of mRNA or cDNA species and pick the most informative probes from that sub-set. The following method describes the use of immobilized oligonucleotide probes (e.g. the probes of the invention) to which mRNA (or related molecules) from different samples is bound to identify which probes are the most informative to identify a particular type of sample, e.g. a disease sample.

The immobilized probes can be derived from various unrelated or related organisms; the only requirement is that the immobilized probes should bind specifically to their homologous counterparts in test organisms. Probes can also be derived from commercially available or public databases and immobilized on solid supports or, as mentioned above, they can be randomly picked and isolated from a cDNA library and immobilized on a solid support.

The length of the probes immobilised on the solid support should be long enough to allow for specific binding to the target sequences. The immobilised probes can be in the form of DNA, RNA or their modified products or PNAs (peptide nucleic acids). Preferably, the probes immobilised should bind specifically to their homologous counterparts representing highly and moderately expressed genes in test organisms. Conveniently the probes which are used are the probes described herein.

The gene expression pattern of cells in biological samples can be generated using prior art techniques such as microarray or macroarray as described below or using methods described herein. Several technologies have now

been developed for monitoring the expression level of a large number of genes simultaneously in biological samples, such as, high-density oligoarrays (Lockhart et al., 1996, Nat. Biotech., 14, p1675-1680), cDNA microarrays (Schena et al, 1995, Science, 270, p467-470) and cDNA macroarrays (Maier E et al., 1994, Nucl. Acids Res., 22, p3423-3424; Bernard et al., 1996, Nucl. Acids Res., 24, p1435-1442).

In high-density oligoarrays and cDNA microarrays, hundreds and thousands of probe oligonucleotides or cDNAs, are spotted onto glass slides or nylon membranes, or synthesized on biochips. The mRNA isolated from the test and reference samples are labelled by reverse transcription with a red or green fluorescent dye, mixed, and hybridised to the microarray. After washing, the bound fluorescent dyes are detected by a laser, producing two images, one for each dye. The resulting ratio of the red and green spots on the two images provides the information about the changes in expression levels of genes in the test and reference samples. Alternatively, single channel or multiple channel microarray studies can also be performed.

In cDNA macroarray, different cDNAs are spotted on a solid support such as nylon membranes in excess in relation to the amount of test mRNA that can hybridise to each spot. mRNA isolated from test samples is radio-labelled by reverse transcription and hybridised to the immobilised probe cDNA. After washing, the signals associated with labels hybridising specifically to immobilised probe cDNA are detected and quantified. The data obtained in macroarray contains information about the relative levels of transcripts present in the test samples. Whilst macroarrays are only suitable to monitor the expression of a limited number of genes, microarrays can be used to monitor the expression of several thousand genes simultaneously and is, therefore,

a preferred choice for large-scale gene expression studies.

A macroarray technique for generating the gene expression data set has been used to illustrate the probe identification method described herein. For this purpose, mRNA is isolated from samples of interest and used to prepare labelled target molecules, e.g. mRNA or cDNA as described above. The labelled target molecules are then hybridised to probes immobilised on the solid support. Various solid supports can be used for the purpose, as described previously. Following hybridization, unbound target molecules are removed and signals from target molecules hybridizing to immobilised probes quantified. If radio labelling is performed, PhosphoImager can be used to generate an image file that can be used to generate a raw data set. Depending on the nature of label chosen for labelling the target molecules, other instruments can also be used, for example, when fluorescence is used for labelling, a FluoroImager can be used to generate an image file from the hybridised target molecules.

The raw data corresponding to mean intensity, median intensity, or volume of the signals in each spot can be acquired from the image file using commercially available software for image analysis. However, the acquired data needs to be corrected for background signals and normalized prior to analysis, since, several factors can affect the quality and quantity of the hybridising signals. For example, variations in the quality and quantity of mRNA isolated from sample to sample, subtle variations in the efficiency of labelling target molecules during each reaction, and variations in the amount of unspecific binding between different macroarrays can all contribute to noise in the acquired data set that must be corrected for prior to analysis.

Background correction can be performed in several

ways. The lowest pixel intensity within a spot can be used for background subtraction or the mean or median of the line of pixels around the spots' outline can be used for the purpose. One can also define an area representing the background intensity based on the signals generated from negative controls and use the average intensity of this area for background subtraction.

The background corrected data can then be transformed for stabilizing the variance in the data structure and normalized for the differences in probe intensity. Several transformation techniques have been described in the literature and a brief overview can be found in Cui, Kerr and Churchill http://www.jax.org/research/churchill/research/ expression/Cui-Transform.pdf). Normalization can be performed by dividing the intensity of each spot with the collective intensity, average intensity or median intensity of all the spots in a macroarray or a group of spots in a macroarray in order to obtain the relative intensity of signals hybridising to immobilised probes in a macroarray. Several methods have been described for normalizing gene expression data (Richmond and Somerville, 2000, Current Opin. Plant Biol., 3, p108-116; Finkelstein et al., 2001, In "Methods of Microarray Data Analysis. Papers from CAMDA, Eds. Lin & Johnsom, Kluwer Academic, p57-68; Yang et al., 2001, In "Optical Technologies and Informatics", Eds. Bittner, Chen, Dorsel & Dougherty, Proceedings of SPIE, 4266, p141-152; Dudoit et al, 2000, J. Am. Stat. Ass., 97, p77-87; Alter et al 2000, supra; Newton et al., 2001, J. Comp. Biol., 8, p37-52). Generally, a scaling factor or function is first calculated to correct the intensity effect and then used for normalising the intensities. The use of external controls has also been suggested for improved normalization.

One other major challenge encountered in large-scale gene expression analysis is that of standardization of data collected from experiments performed at different times. We have observed that gene expression data for samples acquired in the same experiment can be efficiently compared following background correction and normalization. However, the data from samples acquired in experiments performed at different times requires further standardization prior to analysis. This is because subtle differences in experimental parameters between different experiments, for example, differences in the quality and quantity of mRNA extracted at different times, differences in time used for target molecule labelling, hybridization time or exposure time, can affect the measured values. Also, factors such as the nature of the sequence of transcripts under investigation (their GC content) and their amount in relation to the each other determines how they are affected by subtle variations in the experimental processes. They determine, for example, how efficiently first strand cDNAs, corresponding to a particular transcript, are transcribed and labelled during first strand synthesis, or how efficiently the corresponding labelled target molecules bind to their complementary sequences during hybridization. Batch to batch difference in the printing process is also a major factor for variation in the generated expression data.

Failure to properly address and rectify for these influences leads to situations where the differences between the experimental series may overshadow the main information of interest contained in the gene expression data set, i.e. the differences within the combined data from the different experimental series. Figure 1 provides one such example showing a classification based on Principal Component Analysis (PCA) of combined data from two experimental series where the main goal is to

distinguish between Alzheimer/non-Alzheimer patients.

PCA (also known as singular value decomposition) is a technique for studying interdependencies and underlying relationships of a set of variables. data are modelled in terms of a few significant factors or principal components (PC's), plus residuals. PC's contain the main phenomena and define the systematic variability present in the data, while the residuals represent the variability interpreted as noise. Details on PCA can be found in Jollife (1986, Principal Component Analysis, Springer-Verlag, NY), and Jackson (1991, A User's Guide to Principal Components, Wiley, NY). The results of Figure 1 show that two clusters are formed representing the data from two experimental series rather than the Alzheimer/non-Alzheimer differentiation. There were eight samples in common between the two series of experiments, which ideally should have fallen on top of, or in near proximity to, each other if appropriately standardized.

We have now found that gene expression data between different experiments can be efficiently standardized by including a subset of samples from one experimental series in the next experimental series and using a direct standardization method (DS), originally described by Wang and Kowalski (Anal. Chem., 1991, 63, p2750 and J. Chemometrics, 1991, 5, p129-145). Although the method of DS is well known in the field of analytical chemistry, it remains undescribed and unused in the field of gene expression data analysis.

In DS, the secondary data representing for example experimental series 2 (secondary measurements, R_2) are corrected to match the data measured on the primary measurements representing data from series 1 (R_1), while the calibration model remains unchanged. In DS, response matrices for both experimental series are

related to each other by a transformation matrix F, i.e.

$$R_1 = R_2F \tag{1}$$

Where F is a square matrix dimensioned gene by gene. From (1), the transformation matrix is calculated as:

$$F = R_2^+ R_1$$
 (2)

The transformation matrix F in equation (2) is calculated using a relatively small subset of samples which are measured on both the master primary and the secondary series of data.

Finally, the response of the unknown sample measured on the secondary series $r^{\text{\tiny T}}_{2,\,\text{un}}$, is standardized

to the response vector $\mathbf{r}^{^{\mathrm{T}}}_{^{\;1},\,\mathrm{un}}$ expected from the primary series

$$\hat{\mathbf{r}}^{\mathrm{T}}_{1,\mathrm{un}} = \mathbf{r}\mathbf{T}_{21,\mathrm{un}}\hat{\mathbf{F}} \tag{3}$$

From the preceding equation it can be seen that the column i of the transformation matrix contains the multiplication factors for a set of genes measured in the secondary series to obtain the intensity at spot i of the corrected series.

The number of samples that are repeated in the experimental series, R_1 and R_2 , should be equal to their ranks, which in this case is equal to the number of principal components retained for explaining the variation in the R_1 and R_2 . For example, if three principal components are retained for explaining the variation in the data set, a minimum of three samples should be repeated between R_1 and R_2 . The samples that should be repeated between different series should ideally be those that exhibit high leverages in the gene

expression pattern. At times, two samples may suffice, while at other times, more than two samples should be ideally be included for good representativity. In some cases, the samples selected can be the same in all the experimental series to be compared (reference samples), while in other cases, representative samples can be selected sequentially by analyzing the expression pattern after each experiment. The selected samples with high leverages are then included in the next experimental series. The results of using Direct Standardization are shown in Figure 1.

Another approach for normalizing and standardizing the gene expression data set is to hybridize each DNA array with target molecules prepared from a test sample and an equal amount of labelled target molecules prepared from representative reference samples. In order to measure the intensity of labelled target molecules hybridizing to the immobilized probes it is necessary that the labelled molecules are prepared from test and reference samples using different labels, for example, different fluorescent dyes can be used for preparing the labelled material. The labelled molecules prepared from reference samples can be added to the hybridization solution together with the labelled material prepared from test samples. A data file from each array representing the expression pattern of different genes in the test sample and reference samples can then be obtained, normalized and standardized by the direct standardization method as described above. instant advantage of including the differentially labelled target molecules from reference samples during hybridization is that it enables an efficient comparison of new test samples to the data sets already stored in a database.

Monitoring the expression of a large number of genes in several samples leads to the generation of a

large amount of data that is too complex to be easily interpreted. Several unsupervised and supervised multivariate data analysis techniques have already been shown to be useful in extracting meaningful biological information from these large data sets. Cluster analysis is by far the most commonly used technique for gene expression analysis, and has been performed to identify genes that are regulated in a similar manner, and or identifying new/unknown tumour classes using gene expression profiles (Eisen et al., 1998, PNAS, 95, p14863-14868, Alizadeh et al. 2000, supra, Perou et al. 2000, Nature, 406, p747-752; Ross et al, 2000, Nature Genetics, 24(3), p227-235; Herwig et al., 1999, Genome Res., 9, p1093-1105; Tamayo et al, 1999, Science, PNAS, 96, p2907-2912).

In the clustering method, genes are grouped into functional categories (clusters) based on their expression profile, satisfying two criteria: homogeneity - the genes in the same cluster are highly similar in expression to each other; and separation - genes in different clusters have low similarity in expression to each other.

Examples of various clustering techniques that have been used for gene expression analysis include hierarchical clustering (Eisen et al., 1998, supra; Alizadeh et al. 2000, supra; Perou et al. 2000, supra; Ross et al, 2000, supra), K-means clustering (Herwig et al., 1999, supra; Tavazoie et al, 1999, Nature Genetics, 22(3), p. 281-285), gene shaving (Hastie et al., 2000, Genome Biology, 1(2), research 0003.1-0003.21), block clustering (Tibshirani et al., 1999, Tech repot Univ Stanford.) Plaid model (Lazzeroni, 2002, Stat. Sinica, 12, p61-86), and self-organizing maps (Tamayo et al. 1999, supra). Also, related methods of multivariate statistical analysis, such as those using the singular value decomposition (Alter et al., 2000, PNAS, 97(18),

p10101-10106; Ross et al. 2000, supra) or multidimensional scaling can be effective at reducing the dimensions of the objects under study.

However, methods such as cluster analysis and singular value decomposition are purely exploratory and only provide a broad overview of the internal structure present in the data. They are unsupervised approaches in which the available information concerning the nature of the class under investigation is not used in the analysis. Often, the nature of the biological perturbation to which a particular sample has been subjected is known. For example, it is sometimes known whether the sample whose gene expression pattern is being analysed derives from a diseased or healthy individual. In such instances, discriminant analysis can be used for classifying samples into various groups based on their gene expression data.

In such an analysis one builds the classifier by training the data that is capable of discriminating between member and non-members of a given class. trained classifier can then be used to predict the class of unknown samples. Examples of discrimination methods that have been described in the literature include Support Vector Machines (Brown et al, 2000, PNAS, 97, p262-267), Nearest Neighbour (Dudoit et al., 2000, supra), Classification trees (Dudoit et al., 2000, supra), Voted classification (Dudoit et al., 2000, supra), Weighted Gene voting (Golub et al. 1999, supra), and Bayesian classification (Keller et al. 2000, Tec report Univ of Washington). Also a technique in which PLS (Partial Least Square) regression analysis is first used to reduce the dimensions in the gene expression data set followed by classification using logistic discriminant analysis and quadratic discriminant analysis (LD and QDA) has recently been described (Nguyen & Rocke, 2002, Bioinformatics, 18, p39-50 and

1216-1226).

A challenge that gene expression data poses to classical discriminatory methods is that the number of genes whose expression are being analysed is very large compared to the number of samples being analysed. However in most cases only a small fraction of these genes are informative in discriminant analysis problems. Moreover, there is a danger that the noise from irrelevant genes can mask or distort the information from the informative genes. Several methods have been suggested in literature to identify and select genes that are informative in microarray studies, for example, t-statistics (Dudoit et al, 2002, J. Am. Stat. Ass., 97, p77-87), analysis of variance (Kerr et al., 2000, PNAS, 98, p8961-8965), Neighbourhood analysis (Golub et al, 1999, supra), Ratio of between groups to within groups sum of squares (Dudoit et al., 2002, supra), Non parametric scoring (Park et al., 2002, Pacific Symposium on Biocomputing, p52-63) and Likelihood selection (Keller et al., 2000, supra).

In the methods described herein the gene expression data that has been normalized and standardized is analysed by using Partial Least Squares Regression (PLSR). Although PLSR is primarily a method used for regression analysis of continuous data (see Appendix A), it can also be utilized as a method for model building and discriminant analysis using a dummy response matrix based on a binary coding. The class assignment is based on a simple dichotomous distinction such as breast cancer (class 1) / healthy (class 2), or a multiple distinction based on multiple disease diagnosis such as breast cancer (class 1) / Alzheimer (class 2) / healthy (class 3). The list of diseases for classification can be increased depending upon the samples available corresponding to other diseases or conditions or stages thereof.

PLSR applied as a classification method is referred to as PLS-DA (DA standing for Discriminant analysis). PLS-DA is an extension of the PLSR algorithm in which the Y-matrix is a dummy matrix containing n rows (corresponding to the number of samples) and K columns (corresponding to the number of classes). The Y-matrix is constructed by inserting 1 in the kth column and -1 in all the other columns if the corresponding ith object of X belongs to class k. By regressing Y onto X, classification of a new sample is achieved by selecting the group corresponding to the largest component of the fitted, $(x) = (_1(x), _2(x), ..., _k(x))$. Thus, in a -1/1 response matrix, a prediction value below 0 means that the sample belongs to the class designated as -1, while a prediction value above 0 implies that the sample belongs to the class designated as 1.

An advantage of PLSR-DA is that the results obtained can be easily represented in the form of two different plots, the score and loading plots. Score plots represent a projection of the samples onto the principal components and shows the distribution of the samples in the classification model and their relationship to one another. Loading plots display correlations between the variables present in the data set.

It is usually recommended to use PLS-DA as a starting point for the classification problem due to its ability to handle collinear data, and the property of PLSR as a dimension reduction technique. Once this purpose has been satisfied, it is possible to use other methods such as Linear discriminant analysis, LDA, that has been shown to be effective in extracting further information, Indahl et al. (1999, Chem. and Intell. Lab. Syst., 49, p19-31). This approach is based on first decomposing the data using PLS-DA, and then using the scores vectors (instead of the original variables) as

input to LDA. Further details on LDA can be found in Duda and Hart (Classification and Scene Analysis, 1973, Wiley, USA).

The next step following model building is of model validation. This step is considered to be amongst the most important aspects of multivariate analysis, and tests the "goodness" of the calibration model which has been built. In this work, a cross validation approach has been used for validation. In this approach, one or a few samples are kept out in each segment while the model is built using a full cross-validation on the basis of the remaining data. The samples left out are then used for prediction/classification. Repeating the simple cross-validation process several times holding different samples out for each cross-validation leads to a so-called double cross-validation procedure. approach has been shown to work well with a limited amount of data, as is the case in some of the Examples described here. Also, since the cross validation step is repeated several times the dangers of model bias and overfitting are reduced.

Once a calibration model has been built and validated, genes exhibiting an expression pattern that is most relevant for describing the desired information in the model can be selected by techniques described in the prior art for variable selection, as mentioned elsewhere. Variable selection will help in reducing the final model complexity, provide a parsimonious model, and thus lead to a reliable model that can be used for prediction. Moreover, use of fewer genes for the purpose of providing diagnosis will reduce the cost of the diagnostic product. In this way informative probes which would bind to the genes of relevance may be identified.

We have found that after a calibration model has been built, statistical techniques like Jackknife

(Effron, 1982, The Jackknife, the Bootstrap and other resampling plans. Society for Industrial and Applied mathematics, Philadelphia, USA), based on resampling methodology, can be efficiently used to select or confirm significant variables (informative probes).

The approximate uncertainty variance of the PLS regression coefficients B can be estimated by:

$$S^{2}B = \sum_{m=1}^{M} ((B-B_{m})g)^{2}$$

where

 S^2B = estimated uncertainty variance of B;

B = the regression coefficient at the cross validated rank A using all the N objects;

 B_m = the regression coefficient at the rank A using all objects except the object(s) left out in cross validation segment m_i ; and

g = scaling coefficient (here: <math>g=1).

In our approach, Jackknife has been implemented together with cross-validation. For each variable the difference between the B-coefficients B_i in a cross-validated sub-model and B_{tot} for the total model is first calculated. The sum of the squares of the differences is then calculated in all sub-models to obtain an expression of the variance of the B_i estimate for a variable. The significance of the estimate of B_i is calculated using the t-test. Thus, the resulting regression coefficients can be presented with uncertainty limits that correspond to 2 Standard Deviations, and from that significant variables are detected.

No further details as to the implementation or use of this step are provided here since this has been implemented in commercially available software, The

Unscrambler, CAMO ASA, Norway. Also, details on variable selection using Jackknife can be found in Westad & Martens (2000, J. Near Inf. Spectr., 8, p117-124).

The following approach can be used to select informative probes from a gene expression data set:

- a) keep out one unique sample (including its repetitions if present in the data set) per cross validation segment;
- b) build a calibration model (cross validated segment) on the remaining samples using PLSR-DA;
- c) select the significant genes for the model in step b) using the Jackknife criterion;
- d) repeat the above 3 steps until all the unique samples in the data set are kept out once (as described in step a). For example, if 75 unique samples are present in the data set, 75 different calibration models are built resulting in a collection of 75 different sets of significant probes;
- e) select the most significant variables using the frequency of occurrence criterion in the generated sets of significant probes in step d). For example, a set of probes appearing in all sets (100%) are more informative than probes appearing in only 50% of the generated sets in step d).

Once the informative probes for a disease have been selected, a final model is made and validated. The two most commonly used ways of validating the model are cross-validation (CV) and test set validation. In cross-validation, the data is divided into k subsets. The model is then trained k times, each time leaving out one of the subsets from training, but using only the omitted subset to compute error criterion, RMSEP (Root Mean Square Error of Prediction). If k equals the sample size, this is called "leave-one-out" cross-validation. The idea of leaving one or a few samples

out per validation segment is valid only in cases where the covariance between the various experiments is zero. Thus, one sample at-a-time approach can not be justified in situations containing replicates since keeping only one of the replicates out will introduce a systematic bias in our analysis. The correct approach in this case will be to leave out all replicates of the same samples at a time since that would satisfy assumptions of zero covariance between the CV-segments.

The second approach for model validation is to use a separate test-set for validating the calibration model. This requires running a separate set of experiments to be used as a test set. This is the preferred approach given that real test data are available.

The final model is then used to identify a disease, condition or stage thereof in test samples. For this purpose, expression data of selected informative genes is generated from test samples and then the final model is used to determine whether a sample belongs to a diseased or non-diseased class or has a condition or stage thereof.

Thus viewed from a yet further aspect the present invention provides a method of identifying probes useful for diagnosing or identifying or monitoring a disease or condition or stage thereof in an organism, comprising the steps of:

- a) immobilizing a set of oligonucleotide probes, preferably as described hereinbefore, on a solid support;
- b) isolating mRNA from a sample of a normal organism (normal sample), which may optionally be reverse transcribed to cDNA;
- c) isolating mRNA from a sample from an organism, corresponding to the sample and organism of step (b), which is known to have said disease

- or condition or a stage thereof (diseased sample), which may optionally be reverse transcribed to cDNA;
- d) hybridizing the mRNA or cDNA of steps (b) and(c) to said set of immobilized oligonucleotideprobes of step (a); and
- e) assessing the amount of mRNA or cDNA hybridizing to each of said oligonucleotide probes to determine the level of gene expression of genes to which said oligonucleotide probes bind in said normal and diseased samples to generate a gene expression data set for each sample;
- f) normalizing and standardizing said data set of
 step (e);
- g) constructing a calibration model for classification, preferably using the statistical techniques Partial Least Squares Discriminant Analysis (PLS-DA) and Linear Discriminant Analysis (LDA);
- h) performing JackKnife analysis and identifying those oligonucleotide probes which are required for classification of said disease and normal samples into their respective groups.

Preferably a model for classification purposes is generated by using the data relating to the probes identified according to the above described method. Preferably the sample is as described previously. Preferably the oligonucleotides which are immobilized in step (a) are randomly selected as described below or are the probes as described hereinbefore. Such oligonucleotides may be of considerable length, e.g. if using cDNA (which is encompassed within the scope of the term "oligonucleotide"). The identification of such cDNA molecules as useful probes allows the development

of shorter oligonucleotides which reflect the specificity of the cDNA molecules but are easier to manufacture and manipulate.

The above described model may then be used to generate and analyse data of test samples and thus may be used for the diagnostic methods of the invention. In such methods the data generated from the test sample provides the gene expression data set and this is normalized and standardized as described above. This is then fitted to the calibration model described above to provide classification.

The method described herein can also be used to simultaneously select informative probes for several related and unrelated diseases or conditions. Depending upon which diseases or conditions have been included in the calibration or training set, informative probes can be selected for the said diseases or conditions. The informative probes selected for one disease or condition may or may not be similar to the informative probes selected for another disease or condition of interest. It is the pattern with which the selected genes are expressed in relation to each other during a disease, condition, or stage thereof, that determines whether or not they are informative for the disease, condition or stage thereof.

In other words, informative genes are selected based on how their expression correlates with the expression of other selected informative genes under the influence of responses generated by the disease, condition or stage thereof under investigation. In examples 1 and 2 provided hereinafter, 139 informative probes were selected for breast cancer diagnosis and 182 probes were selected for Alzheimer's disease diagnosis by training the gene expression data set of genes representing 1435 or 758 randomly picked cDNA clones for breast cancer/non breast cancer samples, or

Alzheimer/non-Alzheimer samples, respectively. Among the probes selected for breast cancer and Alzheimer, about 10 probes were informative both for breast cancer and Alzheimer disease diagnosis.

For the purpose of isolating informative probes or identifying several related and unrelated diseases, conditions and stages thereof simultaneously, the gene expression data set must contain the information on how genes are expressed when the subject has a particular disease, condition or stage thereof under investigation. The data set is generated from a set of healthy or diseased samples, where a particular sample may contain the information of only one disease, condition or stages thereof or may also contain information about multiple diseases, conditions or stages thereof. For example, if the isolation of informative probes for Alzheimer disease, breast cancer and diabetes is sought, whole blood samples can be obtained from an Alzheimer patient who has breast cancer and diabetes. Hence, the method also teaches an efficient experimental design to reduce the number of samples required for isolating informative probes by selecting samples representing more than one disease, condition or stage thereof.

As mentioned previously, in view of the high information content of most transcripts, the identification and selection of informative probes for use in diagnosing, monitoring or identifying a particular disease, condition or stage thereof may be dramatically simplified. Thus the pool of genes from which a selection may be made to identify informative probes may be radically reduced.

Unlike, in prior art technologies where informative probes are selected from a population of thousands of genes that are being expressed in a cell, like in microarray, in the method described herein, the informative probes are selected from a limited number of

randomly obtained genes. For example, from a population of 1435 cDNA clones, randomly picked from a human whole blood cDNA library, we were able to select 139 informative probes for breast cancer diagnosis (see Example 1 and Table 2).

Thus in a preferred aspect of the above mentioned method of identifying probes useful for diagnosing or identifying or monitoring a disease or condition or stage thereof in an organism, said set of oligonucleotides which are immobilized in step (a) are randomly selected from a larger set of oligonucleotides, e.g. from a cDNA library or other oligonucleotide pool, which may be, but is preferably not selected from the set provided herein. Preferably said larger set comprises oligonucleotides which correspond to moderately or highly expressed genes. Thus preferably in methods of the invention, the set of oligonucleotides according to the invention are replaced with a set of oligonucleotides which are randomly selected, e.g. from commercially available oligonucleotide or cDNA libraries.

As referred to herein "random" refers to selection which is not biased based on the extent of information carried by the transcripts in relation to the disease, condition or organism under study, ie. without bias towards their likely utility as informative probes. Whilst a random selection may be made from a pool of transcripts (or related products) which have been biased, e.g. to highly or moderately expressed transcripts, preferably random selection is made from a pool of transcripts not biased or selected by a sequence-based criterion. The larger set may therefore contain oligonucleotides corresponding to highly and moderately expressed genes, or alternatively, may be enriched for those corresponding to the highly and moderately expressed genes.

Random selection from highly and moderately expressed genes can be achieved in a wide variety of ways. A strategy used in this work, but not limiting in itself involves randomly picking a significant number of cDNA clones from a cDNA library constructed from a biological specimen under investigation. Since, in a cDNA library, the cDNA clones corresponding to transcripts present in high or moderate amount are more frequently present than transcripts corresponding to cDNA present in low amount, the former will tend to be picked up more frequently than the latter. A pool of cDNA enriched for those corresponding to highly and moderately expressed genes can be isolated by this approach.

To identify genes that are expressed in high or moderate amount among the isolated population for use in methods of the invention, the information about the relative level of their transcripts in samples of interest can be generated using several prior art techniques. Both non-sequence based methods, such as differential display or RNA fingerprinting, and sequence-based methods such as microarrays or macroarrays can be used for the purpose. Alternatively, specific primer sequences for highly and moderately expressed genes can be designed and methods such as quantitative RT-PCR can be used to determine the levels of highly and moderately expressed genes. Hence, a skilled practitioner may use a variety of techniques which are known in the art for determining the relative level of mRNA in a biological sample.

Especially preferably the sample for the isolation of mRNA in the above described method is as described previously and is preferably not from the site of disease and the cells in said sample are not disease cells and have not contacted disease cells.

The following examples are given by way of

illustration only in which the Figures referred to are as follows:

Figure 1 shows the effect of Direct Standardization (DS) on the Alzheimer data measured in two different series of experiments in which AD denotes Alzheimer's samples and A,B are non-Alzheimer's samples. samples in both series have been labelled systematically as (xx 7/xx 8), whereas the corrected samples from series 8 (in b,c,d) have been labelled as (xx c), thus, for example, AD2-7 denotes Alzheimer disease sample number 2 in experiment series 7. The circled spots represent the samples chosen as the transfer samples. The connecting lines in figures b,c,d show the proximity of the replicated samples after applying DS. The dashed lines in figures a,c,d represent the decision boundary separating the classes. These lines have not been drawn on the basis of any statistical criteria, but serve the purpose of visually separating the classes. All the four figures show scores plot (PC1-PC2) from PCA analysis based on (a) non-standardized data, (b) scores plot after direct standardization using 3 transfer samples, (c) scores plot after direct standardization using 4 transfer sample, (d) scores plot after direct standardization using 8 transfer samples;

Figure 2 shows the projection of normal (including benign) and breast cancer samples onto a classification model generated by PLSR-DA using the data of 44 informative genes, in which PC is the principal components and N and C are normal and breast cancer samples, respectively;

Figure 3 shows the projection of individuals with and without Alzheimer's disease onto a classification model generated by PLSR-DA using 182 informative genes;

Figures 4, 6 and 8 show projection plots as Figure 2 in which the classification model is generated using 719, 111 and 345 cDNAs, respectively, wherein PC is the

principal components, N denotes normal and B denotes breast cancer samples;

Figures 5, 7 and 9 show prediction plots based on 3 principal components using the data of 719, 111 and 345 cDNAs, respectively;

 $\underline{\text{Figure 10}}$ shows a projection plot as Figure 3 in which the classification model is generated using 520 cDNAs; and

 $\underline{\text{Figure 11}}$ is the prediction plot corresponding to Figure 10.

Example 1: Diagnosis of Breast Cancer

Methods

Whole blood was obtained from the arms of breast cancer patients and patients with benign tumours (Ullevål and Haukland hospitals in Norway). All of the patients with breast cancer had a malignant tumour of the breast (disease samples). Healthy blood was collected from the above two hospitals, or collected at a Health station at Ås, Norway or at DiaGenic AS, Norway, from the arms of female donors with no reported signs of breast cancer. The blood from healthy individuals or with benign tumours comprise the normal samples. The blood was either collected in tubes containing EDTA and stored immediately at -80°C or was collected in PAXgene tubes and stored for 12-24 hours at room temperature before finally storing them at -80° C before use. Further details of the breast cancer and benign tumour patients from which blood was taken is provided in Table 5.

mRNA was isolated from the blood of the 29 breast cancer patients and 46 normal donors and used to prepare labelled probes by reverse transcribing in the presence of $\alpha^{33}P\text{-}dATP$. The first strand cDNA of the normal and

diseased samples was bound, separately to 1435 cDNA clones immobilized on a solid support (nylon membrane). These cDNA clones were randomly picked, without any prior knowledge of their gene sequences, from a cDNA library constructed using whole blood of 550 healthy individuals (Clontech, Palo Alto, USA). These methods were conducted as follows.

For amplification of inserts, bacterial clones were grown in microtiter plates containing 150 µl LB with 50 μg/ml carbenicillin, and incubated overnight with agitation at 37°C. To lyse the cells, $5 \mu l$ of each culture were diluted with 50 μ l H2O and incubated for 12 min. at 95° C. Of this mixture, 2 μ l were subjected to a PCR reaction using 20 pmoles of M13 forward and reverse primer in presence of 1.5 mM MgCl_2 . PCR reactions were performed with the following cycling protocol: 4 min. at 95°C, followed by 25 cycles of 1 min. at 94°C, 1 min. at 60°C and 3 min. at 72°C either in a RoboCycler® Temperature Cycler (Stratagene, La Jolla, USA) or DNA Engine Dyad Peltier Thermal Cycler (MJ Research Inc., Waltham, USA). The amplified products were denatured by incubating with NaOH (0.2 M, final concentration) for 30 min. and spotted onto Hybond-N+ membranes (Amersham Pharmacia Biotech, Little Chalfont, UK), using MicroGrid II workstation according to the manufacturer's instructions (BioRobotics Ltd, Cambridge England). The immobilized cDNAs were fixed using a UV cross-linker (Hoefer Scientific Instruments, San Francisco, USA).

In addition to the 1435 cDNAs, the printed arrays also contained controls for assessing background level, consistency and sensitivity of the assay. These were spotted at multiple positions and included controls such as PCR mix (without any insert); positive and negative controls of SpotReportTM 10 array validation system

(Stratagene, La Jolla, USA) and cDNAs corresponding to constitutively expressed genes such as b-actin, g-actin, GAPDH, HOD and cyclophilin. Also, oligonucleotides corresponding to SIX1, b-tubulin, TRP-2, MDM2, Myosin Light C, CD44, Maspin, Laminin, and SRP 19 were included to detect disseminated cancer cells.

The total RNA from blood collected in EDTA tubes was purified using Trizol LS Reagent protocol (Invitrogen/Life Technologies). From blood contained in PAXgene tubes, the total RNA was purified according to the supplier's instructions (PreAnalytiX, Hombrechtikon, Switzerland). Contaminating DNA was removed from the isolated RNA by DNAase I treatment using DNA-free kit (Ambion, Inc. Austin, USA). RNA quality was determined visually by inspecting the integrity of 28S and 18S ribosomal bands following agarose gel electrophoresis. The concentration and purity of extracted RNA was determined by measuring the absorbance at 260 nm and 280 nm. mRNA was isolated from the total RNA using Dynabeads as per the supplier's instructions (Dynal AS, Oslo, Norway).

Labelling and hybridization experiments were performed in batches. The number of samples assayed in each batch varied from six to nine. In the case of samples that were assayed more than once (replicates), aliquots derived from the same mRNA pool were used for probe synthesis. For probe synthesis, aliquots of mRNA corresponding to 4-5 μg of total RNA were mixed together with oligodT_{25NV} (0.5 $\mu g/ml$) and mRNA spikes of SpotReport 10 array validation system (10 pg; Spike 2, 1 pg), heated to 70°C to remove secondary structures, and then chilled on ice. Probes were prepared in 35 μl reaction mixes by reverse transcription in the presence of 50 μ Ci [α^{33} P] dATP, 3.5 μ M dATP, 0.6 mM each of dCTP,

dTTP, dGTP, 200 units of SuperScript reverse transcriptase (Invitrogen, LifeTechnologies) and 0.1 M DTT, labelling for 1.5 hr at 42°C. Following synthesis, the enzyme was deactivated for 10 min. at 70°C and mRNA removed by incubating the reaction mix for 20 min. at 37°C in 4 units of Ribo H (Promega, Madison USA). Unincorporated nucleotides were removed using ProbeQuant G 50 Columns (Amersham Biosciences, Piscataway, USA).

Prior to hybridization, the membranes were equilibrated in 4 x SSC for 2 hr at room temperature and prehybridized overnight at 65°C in 10 ml prehybridisation solution (4 x SSC, 0.1 M NaH₂PO₄, 1 mM EDTA, 8% dextran sulphate, 10 x denhardt's solution, 1% SDS). Freshly prepared probes were added to 5 ml of the same prehybridisation solution, and hybridization continued overnight at 65°C. The membranes were washed at 65°C at increasing stringency (2 x 30 min. each in 2 x SSC, 0.1% SDS; 1 x SSC, 0.1% SDS; 0.1 x SSC, 0.1% SDS) to remove unspecific signals.

The amount of labelled first strand cDNA binding to each spot was assessed and quantified using a Phospholmager to generate a gene expression data set. The data was generated using Phoretix software version 3 (Non Linear Dynamics, England). Background subtraction was performed on the generated data by subtracting the median of the line of pixels around each spot outline from the total intensity obtained from the respective spots.

The background-subtracted data was then normalized and transformed by selecting out 50 lowest and 50 maximum signals from each membrane. This step was to exclude genes that were expressed with a high degree of variance. Since the genes varied from membrane to

membrane, the expression data from 497 genes were removed from the data set. The values for the remaining 938 genes were then normalised by using different approaches such as external controls, dividing each spot by the median intensity of the observed signal in the respective membrane, range normalizing the data from each membrane, and then log transforming the data obtained.

The processed data obtained above was then used to isolate the informative probes by:

- a) keeping one unique sample (including all repetitions of the selected sample) out per cross validation segment;
- b) building a calibration model (cross validated) on the remaining samples using PLSR-DA;
- c) selecting the set of significant genes for the model in step b using the Jackknife criterion;
- d) repeating steps a), b) and c) until all the unique samples were kept out once (hence, in all 75 different calibration models were built (after repeating step b) 75 times), resulting in 75 different sets of significant probes (after repeating step c) 75 times));
- e) selecting significant variables using the frequency of occurrence criterion amongst the 75 different sets of significant probes.

The selected informative probes based on occurrence criterion were used to construct a classification model. The result of the classification model based on probes appearing in at least 90% of the generated sets after the step of isolating informative probes as described above is shown in Figure 2 in which it is seen that the expression pattern of these genes was able to classify most women with breast cancer and women with no breast cancer into distinct groups. In this figure PC1 and PC2

indicate the two principal components statistically derived from the data which best define the systemic variability present in the data. This allows each sample, and the data from each of the informative probes to which the sample's labelled first strand cDNA was bound, to be represented on the classification model as a single point which is a projection of the sample onto the principal components - the score plot.

The ability of the generated model, based on isolated informative probes, to predict future samples was determined by the double cross-validation approach. The performance of the diagnostic test for breast cancer based on the occurrence criterion is presented in Table 6.

Correct prediction of most breast cancer cells was achieved. These included all three samples obtained from women with ductal carcinoma in situ (DCIS), 11/15 samples obtained from women with stage I breast cancer, all five samples obtained from women with stage II breast cancer, and one of two samples obtained from women with stage III breast cancer. Interestingly, two correctly predicted stage I samples were obtained from women having a tumour size of <5 mm in diameter.

The model also correctly predicted the class of most non-cancer samples (41/46), including those that were obtained from women with non-cancerous breast abnormalities.

Confirmation that the gene transcripts are not from cells which are disseminated disease cells has been confirmed by several lines of evidences. Firstly, the informative genes were expressed constitutively at high or moderate levels in blood cells of women irrespective

of whether they had cancer or not. Secondly, in the assay described in this Example, in order to identify transcripts, at least 720 disseminated cells in blood samples would be required. Since, the average number of disseminated cells present in blood during different stages of breast cancer is much lower (organ confined breast cancer, 0.8 cells per ml; invasive breast cancer spread to lymph nodes only, 2.4 cells per ml; and metastatic breast cancer, 6 cells per ml; SD>100%) (29), we believe that the signals being detected originated from peripheral blood cells and could not have originated from disseminated cells. Thirdly, we were not able to detect any signal from the eight cancer markers known to have elevated expression in malignant cancer cells, including cancer cells that are disseminated in the blood.

Example 2: Diagnosis of Alzheimer's disease

Similar experiments were conducted with samples from Alzheimer's patients. In this method 7 patients diagnosed with Alzheimer's Disease at the Memory Clinic at Ullevål University Hospital were used in the trial. The patients were confirmed as having Alzheimer's disease based on the following criteria:

- * A standardized interview with a care-giver using IQCODE, an ADL scale and a scale measuring behaviour of the patient (Green scale).
- * Neuropsychological evaluation using MMSE, Clock drawing test, Trailmaking test A and B (TMT A and B), Kendrick object learning test (visual memory test), part of the Wechsler battery and Benton test.
- * A psychiatric evaluation using scales for detection of depression, MADRS for interviewing the patient and Cornell scale for interviewing the care-giver.

- * A physical examination.
- * Laboratory tests of blood samples to rule out other diseases.
- * CT scan of the brain.
- * SPECT of the brain.

The mean age of the patients was 72.3 with an age range of 69-76. The mean MMSE score was 22.0 (the maximum score attainable being 30).

Six age-matched individuals without diagnosed Alzheimer's disease were used as a control. All had been tested with MMSE and had a minimum score of 28 (mean: 28.4). The mean age of the normal control group was 73.0 and the age range 66-81. A sample from a 16-year old individual, with a consequent minimal chance of having Alzheimer's disease, was also included as an additional control.

Using the methods described above (except that hybridization to 758 rather than 1435 cDNA clones was performed), informative probes were selected based on occurrence criterion and used to construct a classification model. The results of the classification model based on probes appearing at least once in the generated sets after the method to isolate informative probes as described above is shown in Figure 3 in which it will be seen that the expression pattern of these genes was able to classify individuals with or without Alzheimer's disease into distinct groups. In this Figure PC1 and PC2 indicate the 2 principal components statistically derived from the data which define the systematic variability present in the data. each sample, and the data from each of the informative probes to which the samples' cDNA was bound, to be represented on the classification model as a single

point which is a projection of the sample onto the principal components - the score plot.

The ability of the generated model, based on isolated informative probes, to predict future samples was determined by the double cross-validation. The performance of the diagnostic test for Alzheimer's disease is presented in Table 7.

Appendix A

Partial Least Squares regression (PLSR)

Let a multivariate regression model be defined as:

Y = XB + F

where

X a NxP matrix with N predictor variables (genes); Y (NxJ) being the J predicted variables. In our case Y represents a matrix containing dummy variables; B is a matrix of regression coefficients; and F is a NxJ matrix of residuals.

The structure of the PLSR model can be written as:

 $X = TP^{T} + E_{A}$, and $Y = TQ^{T} + F_{A}$, where

where

T (NxA) is a matrix of score vectors which are linear combinations of the x-variables;

P (PxA) is a matrix with the x-loading vectors p_a as columns;

Q (JxA) is a matrix with the y-loading vectors q_a as columns;

 E_a (NxP) is the matrix for X after A factors; and F_a (NxJ) is the matrix for Y after A factors.

The criterion in PLSR is to maximize the explained covariance of [X,Y]. This is achieved by the loading weights vector w_{a+1} , which is the first eigenvector of $E_a{}^TF_aF_a{}^TE_a$ (E_a and F_a are the deflated X and Y after a factors or PLS components).

The regression coefficients are given by: $B \ = \ \textbf{W} \, (\, P^T \textbf{W})^{\, -1} Q^T$

A PLSR model with full rank, i.e. maximum number of components, is equivalent to the MLR solutions. Further details on PLSR can be found in Marteus & Naes, 1989, Multivariate Calibration, John Wiley & Sons, Inc., USA and Kowalski & Seasholtz, 1991, supra.

Example 3: Validation of Example 1, diagnosis of breast cancer

The results in Example 1 were validated by using the informative probes identified in Example 1 on new beast cancer and control samples.

Methods

The methods, essentially as described in Example 1, were used. Blood was taken from patients as described in Table 8. However, blood was collected in PAXgene tubes and the first strand labelled cDNAs were hybridized to 719 cDNAs spotted on nylon membranes along with other controls as described in Example 1. After background subtraction using control spots, the data of each membrane was normalized using the inter quantile range. The data was analysed as described in Example 1 and the model validated by cross validation.

The 719 cDNAs which were spotted are a subset of the cDNAs spotted in Example 1 and include 111 cDNAs described in Table 2 and which were found to be informative in Example 1.

Results

The results are shown in Figures 4 to 9. Figures 4, 6 and 8 are projection plots similar to Figure 2 and show the projection of normal and breast cancer patients' samples onto a classification model generated using all 719 cDNA. Figure 6 is similar but uses a classification model generated with the 111 probes common to Example 1. Figure 8 uses the 345 sequences of the 719 for which sequence information is provided herein. In each case classification of normal and breast cancer groups was possible. Figures 5, 7 and 9 show prediction plots which reflect the ability of the generated models to

correctly diagnose breast cancer. In the 3 prediction plots shown, the disease samples appear on the x axis at +1 and the non-disease samples appear at -1. The y axis represents the predicted class membership. During prediction, if the prediction is correct, disease samples should fall above zero and non-disease samples should fall below zero. In each case almost all samples are correctly predicted.

Example 4: Validation of Example 2, diagnosis of Alzheimers

The results in Example 2 were validated by using the informative probes identified in Example 2 on new Alzheimer's patient samples.

Methods

The methods, essentially as described in Example 2, were used. Twelve female patients diagnosed with Alzheimer's disease at the Memory Clinic at Ullevål University Hospital who were confirmed as having Alzheimer's disease based on the criteria of Example 2 were used in the trial. The mean age of the patients was 72.3 with an age range of 66-83. The mean MMSE score was 22.0 (the maximum score attainable being 30).

Sixteen age-matched female individuals without diagnosed Alzheimer's disease were used as the normal control group. All had been tested with MMSE and had a minimum score of 29. The mean age of the normal control group was 74.0 and the age range 66-86.

After transfer of the blood to PAXgene tubes, total mRNA was isolated from the blood of the Alzheimer's disease and from the control group donors according to the manufacturers's instructions (PreAnalytiX,

Hombrechtikon, Switzerland). The isolated mRNA was labelled during reverse transcription in the presence of $\alpha^{33}\text{P-dATP}$, yielding a labelled first strand cDNA. Hybridization was performed as described previously onto 730 cDNA clones picked from a cDNA library from whole blood of 550 healthy individuals without knowledge of the gene sequence of the random cDNA clones.

Results

The results are shown in Figures 10 and 11. Figure 10 is a projection plot generated using 520 probes which have been sequenced. Figure 11 is a prediction plot and shows correct prediction of almost all samples.

List of probes informative for disease diagnosis

Table 1a

	Clone ID	Sequence ID	No. of nucleotides	SEQ ID NO: in sequence listing
1	1-01	_	_	
2	1-02	-	-	
3	I-13	_	-	
4	I-21	_	-	
5 1	I-24	308	373	11
6 2	I-28	310	564	<u>13</u>
7 3	I-30	1180	622	398
<u>84</u>	I-34	313	554	<u>15</u>
9	I-37	_	-	
10	I-12	_	-	
11	I-62	_	-	
12 5	I-54	1181	156	399
13 6	I-58	326	554	24
11	I-71	_	-	
15	I-72	_	-	
16	I-86	_	-	
17	I-95	_	_	
18 7	II-03	361	622	34
19 8	II-05	363	628	<u>35</u>
20 9	II-06	364	528	<u>36</u>
21 10	II-10	368	329	<u>39</u>
22 11	II-24	381	534	47
23 12	II -2 5	382	444	48
24 13	II-26	383	566	<u>49</u>
25 14	II-33	390	523	<u>55</u>
26 15	II-34	391	566	<u>56</u>
27 16	II-41	397	534	<u>60</u>
				61

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28 17	II-42	398	512	
29	II-47	_	_	
30 18	II-57	411	505	<u>73</u>
31 19	II-61	415	596	<u>77</u>
32 20	II-69	423	387	<u>85</u>
33 <u>21</u>	II-70	424	420	<u>86</u>
34 22	II-75	429	535	91
35	II-83	_	_	
36 23	II-84	438	577	<u>99</u>
37 24	II-87	441	552	100
38 25	II-88	442	606	<u>101</u>
39	II-90	-	_	
40 26	II-94	448	329	104
41 27	III-02	453	747	107
42	III-05	-	-	
4328	III-06	458	682	109
4429	III-08	460	536	111
45	III-10	-	-	
46 30	III-13	464	615	115
47	III-15	_	_	
48	III-17	-	-	
49 31	III-20	1183	479	401
50 32	III-23	473	694	119
51 33	III-26	476	476	122
52 34	III-35	485	551	130
53 35	III-39	487	224	131
54 36	III-40	488	349	132
55 37	III-43	490	382	500
56 38	III-44	491	382	134
57 39	III-53	500	390	142
58 40	III-56	503	109	144
59 41	III-57	504	374	145
60	III-60	556	325	

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61	III-60	-	-	18 100
62 42	III-61	507	521	148
63 43	III-63	509	575	<u>150</u>
64	III-68	-	-	
65 44	III-74	518	502	<u>155</u>
66 45	III-80	523	585	<u>158</u>
67	III-82	_	-	
68 46	III-85	526	516	<u>161</u>
69 47	III-89	530	660	<u>165</u>
70	III-92	_	_	
71	III-96	_	_	
72 48	IV-14	684	545	275
73 49	IV-15	1185	628	402
74	IV-23	_	_	
76 50	IV-26	1186	494	403
75	IV-26	_	-	
77	IV-29	_	-	
78 51	IV-31	687	268	278
79 52	IV-32	688	569	279
80	IV-34	_	-	
81	IV-35	_	_	
82	IV-41	_	_	
83	IV-45	_	_	
84 53	IV-53	61	362	498
85	IV-62	-	-	
86 54	IV-69	192	286	4
87 55	IV-80	701	579	<u>291</u>
88	IV-82	-	-	
89	IV-93	-	_	
90 56	IX-10	736	641	314
91	IX-12	-	-	
92 57	IX-38	757	583	317
93 58	IX-39	758	424	318

Marked-Up Copy 94 IX-42 _ _ 319 9559 IX-48 764 626 325 IX-77 785 9660 556 V-01 97 98 V-02 _ 296 V-03 706 9961 496 297 10062 V-04 707 397 101 V-06 298 708 10263 V-07 293 404 10364 V-11 1188 599 301 10465 711 V-12 498 105 V-15 106 V-17 107 V-21 108 V-25 _ _ 109 V-32 V-35 110 V-39 111 112 V-12 _ 113 V-43 114 V-17 115 V-49 V-52 116 _ _ 117 V-54 499 11866 V-55 77 421 119 V-58 120 V-59 121 V-65 122 V-68 123 V-71 124 V-75 V-79 125 311 12667 V-80 726 260

		- 78	_	
127	V-90	_		Marked-Up Copy
128	V-91	_	_	
129	V-92	_	_	
	V-94	_	_	
131	VI-02	_	_	
132 68	VI-04	865	122	222
133 69	VI-07	93	405	339 <u>1</u>
134	VI-09	_	_	_
135	VI-10	_	_	
136 70	VI-12	- 869	667	341
		809 871		343
137 <u>71</u> 138	VI-14		642	
	VI-17	-	-	346
139 72	VI-20	876	115	340
140	VI-21	-	-	347
141 <u>73</u>	VI-23	878	634	347
142	VI-34	_	_	
143	VI-41	_	-	
144	VI-12	-	-	
145	VI-43	-	-	
146	VI-44	_	-	
147 74	VI-48	891	626	<u>355</u>
148	VI-49	-	-	
149 75	VI-50	893	585	<u>356</u>
150	VI-52	_	_	
151 76	VI-53	895	560	<u>357</u>
152 77	VI-55	897	509	<u>359</u>
153	VI-65	-	-	
154 78	VI-70	108	550	2
155	VI-71	-	-	
156	VI-72	_	_	
157 79	VI-74	905	655	365
158 80	VI-76	907	582	367
	VI-78	-	-	
	-			+

				Marked-Up Copy
160	VI-79	-	_	197 (198)
161	VI-84	-	_	
162 81	VI-87	911	595	<u>370</u>
163 82	VI-88	912	651	<u>371</u>
164	VI-90	-	-	
165	VI-93	-	-	
166 83	VI-95	915	230	374
167	VI-96	_	-	
168	VII-02	-	-	
169 84	VII-03	1196	412	411
170	VII-06	-	-	
171	VII-10	-	_	
172	VII-11	_	-	
173 85	VII-15	1199	439	414
174 86	VII-19	562	580	<u>171</u>
175 87	VII-21	564	671	<u>173</u>
176	VII-25	-	-	
177 88	VII-32	571	457	<u>179</u>
178 89	VII-36	575	209	<u>182</u>
179 90	VII-39	576	541	<u>183</u>
180 91	VII-42	579	502	<u>186</u>
181 92	VII-43	580	316	187
182 93	VII-46	583	631	190
183 94	VII-47	1200	526	415
184 95	VII-48	1201	613	416
185 96	VII-59	593	565	199
186	VII-60	-	_	
187 97	VII-63	595	98	201
188 98	VII-66	598	362	204
189	VII-67	-	_	
190 99	VII-72	600	595	206
191 100	VII-73	601	522	207
192	VII-75	-	-	
				209

				Marked-Up Copy
193 101	VII-76	603	624	197 199
194 102	VII-77	1203	692	418
195 103	VII-80	605	338	210
196 104	VII-81	606	556	211
197	VII-83	-	-	
198	VII-86	_	-	
199	VII-88	-	-	
200 105	VII-90	612	576	216
201 106	VII-91	613	341	217
202 107	VII-93	615	379	219
203	VIII-01	_	_	
204	VIII-02	-	-	
205	VIII-03	_	-	
206	VIII-06	_	-	
207 108	VIII-09	618	598	221
208	VIII-10	_	_	
209	VIII-15	_	_	
210 109	VIII-20	628	419	229
211	VIII-22	-	_	
212	VIII-26	_	-	
213 110	VIII-28	634	511	235
214 111	VIII-29	635	592	<u>236</u>
215 112	VIII-30	636	572	237
216 113	VIII-31	637	482	238
217 114	VIII-32	638	545	239
218 115	VIII-33	639	624	240
219	VIII-39	-	-	
220 116	VIII-41	645	649	245
221 117	VIII-42	646	600	246
222	VIII-44	-	-	
223 118	VIII-46	649	425	249
224 119	VIII-48	651	251	251
225	VIII-58	-	-	
				261

Marked-Up Copy 226120 VIII-64 663 627 227 VIII-65 262 228121 VIII-66 665 345 263 229122 VIII-67 666 252 230 VIII-74 270 231123 VIII-76 675 691 232 VIII-78_ _ 233 VIII-82 VIII-83 234 _ _ VIII-85 235 236 VIII-87 _ _ 237 VIII-91 238 $\frac{\text{VIII}-92}{}$ 239 VIII-93 VIII-95 240 _ _ 241 X-04 328 242124 X-07 808 641 329 243125 X-15 814 132 331 X-29 821 244126 370 X-34 245 246 X-35 _ _ 334 837 247127 X-54 603 335 248128 X-56 839 71 421 1207 249129 X-68 642 336 849 250130 X - 72622 337 251131 X-94 860 601 252 XI-07 423 253132 XI-13 1209 620 254 XI-50 255 XI-58 426 256133 XI-81 1212 374 427 257134 XII-07 1213 567 258 XII-17

		02		Marked-Up Copy
259	XII-26	-	-	197 199
260	XII-27	-	-	
261	XII-31		_	
262	XII-32	-	-	
263 135	XII-35	1214	620	428
264	XII-36	_	_	
265	XII-52	_	_	
266 136	XII-59	1216	484	430
267 137	XIII-19	1219	559	433
268	XIII-29	_	_	
269 138	XIII-52	939	513	<u>378</u>
270	XIII-62	-	_	
271	XIII-84	_	_	
272 139	XIII-92	1221	741	435
273	XV-18	-	-	
274 140	XV-22	-	-	388
275	XV-24	_	-	
276 141	XV-25	1224	485	436
277	XV-28	-	-	
278	XV-34	-	-	
279	XV-12	-	_	
280	XV-68	-	-	
281	XV-74	-	-	
282	XV-93	-	_	
283	XV-94	-	-	
284	XV-96	-	-	
285 142	XVI-36	1056	435	382
286 143	XVI-53	1230	741	439
287	XVI-59	_	-	
288 144	XVI-66	1074	689	384
289 145	XVI-76	1083	198	386
290 146	XVI-77	1084	198	387
291	XVII-07	-	-	

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292	XVII-08	_	_	
293	XVII-17	-	-	
294	XVII-28	_	_	
295	XVII-29	-	-	
296 147	XVII-31	1139	503	<u>392</u>
297	XVII-36	-	-	
298	XVII-39	-	-	
299 148	XVII-40	1231	203	440
300 149	XVII-48	1148	587	<u>393</u>
301	XVII-55	-	_	
302	XVII-58	-	_	
303	XVII-67	_	_	
304	XVII-72	_	_	
305 150	XVII-76	1160	650	<u>394</u>
306	XVII-82	-	-	
307 151	XVII-87	1165	502	<u>395</u>
308 152	XVII-95	1172	648	<u>396</u>

Clone ID	Sequence IDSEQ ID
	NO. in Sequence Listing
I-09	298
I-10	299 6
I-13	1331444
I-14	1178 397
I-15	3007
I-16	301
I-17	302 8
I-19	3049
I-20	305
I-22	306 10
I-23	307
I-24	308 11
I-25	309 12
I-28	310 13
I-30	1180 398
I-31	311 14
I-32	312
I-34	313 15
I-37	1440 482
I-38	31416
I-39	315 17
I-40	316 18
I-42	1332 445
I-11	317
I-45	318
I-46	319
I-47	320
I-48	321 19
I-49	322 20
I-53	323 21
I-54	1181 399
I-56	32422
I-57 I-58	325 23 326 24
	327 25
I-60 I-64	321 25 328 26
I-67	330 27
I-69	33128
I-71	332
I-72	333
1-73	334
I-77	335 29
I-79	336
I-80	337 30
I-81	338 31
1-82	339 32
I-86	1336447
I-88	1182400
I-95	1337448
II-02	360 33
II-03	361 34
II-05	363 35
II-06	36436
II-07	365 37
II-08	366 38
11-09	367
II-10	368 39
II-11	369 40
II-12	370 41
II-13	371 42
II-14	372
II-15	373 43
II-16	37444

II-17	375
	1
II-18	376
II-20	377
II-21	378 45
II-22	379
II-23	380 46
II-24	38147
	0.000
II-25	382 48
II-26	38349
II-27	384 50
II-28	385
II-29	386 51
II-30	387 52
II-31	388 53
	389 54
II-32	
II-33	390 55
II-34	391 56
II-35	392
II-37	393
II-38	394 57
II-39	395 58
II-40	396 59
II-41	397 60
II-42	398 61
II-43	399 62
11-40	
II-44	400 63
II-46	40164
	402 65
II-47	
II-48	403 66
II-49	404
II-50	405 67
II-52	406 68
II-53	40769
II-54	408 70
II-55	409 71
II-56	110 72
II-57	411 73
II-58	412 74
II-59	413 75
II-60	414 76
II-61	415 77
II-62	416 78
II-63	417 79
	418 80
II-64	
II-65	419 81
II-66	420 82
II-67	421 83
II-68	422 84
II-69	423 85
II-70	42486
II-71	425 87
II-72	126 88
II-73	427 89
II-74	428 90
II-75	429 91
II-76	430 92
II-77	43193
II-78	43294
II-79	433 95
II-80	43496
	1
II-81	435 97
II-82	436 98
11 02 11-83	437
II-84	438 99
II-85	439
II-86	440
II-87	441 100
II-88	442101
II-89	443
II-90	444
II-91	445
II-92	446 102
II-93	447103
	1

II-94	448104
11-95	449
II-96	450 105
III-01	452 106
III-02	453 107
III-03	454 108
III-04	455
111-01	457
III-06	458109
III-06	458109 459110
III-08	460111
III-09	461 112
III-11	462 113
III-12	463 114
III-13	464 115
III-14	465
III-15	466
III-16	467
III-17	468
III-18	469 116
III-19	470
III-20	1183 401
III-21	471 117
III-22	472 118
III-22 III-23	473 119
III-23 III-24	474 120
III-24 III-25	474120 475121
III-26	476122 477123
III-27	
III-28	478124
III-29	479 125
III-31	481 126
III-32	482 127
III-33	483 128
III-34	484 129
III-35	485 130
III-37	486
III-39	487 131
III-40	488 132
III-42	489 133
III-43	490 500
III-44	491 134
III-45	492 135
III-46	493 136
III-40 III-47	494 137
III-48	495 138
III-48 III-49	495 138 496 139
III-50	497140
III-51	498
III-52	499141
III-53	500 142
III-54	501
III-55	502 143
III-56	503 144
III-57	504 145
III-58	505 146
III-59	506 147
III-61	507 148
III-62	508 149
III-63	509 150
III-64	510 151
III 65	511
III-66	512 152
III-66	512 152 513 153
III-69	514
III-70	515 154
III-71	516
III-73	517
III-74	518 155
III-76	519 156
III-77	520
III-78	521 157
	522
III-79	522

	1
III-80	523 158
III-81	524 159
III-82	1348 451
III-83	525 160
III-85	526 161
III-86	527 162
III-87	528
III-88	529 163 & 164
III-89	530 165
III-91	531
III-92	1351 452
III-93	532 166
III-94	533 167
III-95	534 168
III-96	535
IV-02	681
IV-04	682 273
IV-13	683 274
IV-14	684 275
IV-15	1185 402
IV-17	685 276
IV-23	1353 454
IV-26	1186 403
IV-28	686 277
IV-31	687 278
IV-32	688 279
IV-35	1355 455
IV-37	α6 497
	689 280
IV-38	
IV-40	690 281
IV-42	691 282
IV-43	1239441
IV-44	
	692 283
IV-47	693 284
IV-53	61 498
IV-55	694 285
IV-56	695
IV-61	696 286
IV-64	697 287
IV-65	698 288
	1924
IV-69	
IV-72	699 289
IV-73	700 290
IV-80	701 291
IV-82	196
IV-85	702 292
IV-93	703 293
TV-95	704294
IV-96	705 295
IX-10	736 314
IX-12	738
IX-13	739 315
IX-24	747316
IX-38	757 317
IX-39	758 318
IX-48	764 319
IX-50	766 320
IX-56	768 321
IX-62	773 322
IX-65	776 323
IX-72	782 324
IX-77	785 325
IX-91	796 326
IX-96	801 327
V-01	1361 458
	706 296
V-03	
V-03 V-04	707 297
V-04	
V-04 V-07	708 298
V-04 V-07 V-08	708 298 709 299
V-04 V-07	708 298
V-04 V-07 V-08 V-09	708 298 709 299
V-04 V-07 V-08 V-09 V-11	708298 709299 710300 1188404
V-04 V-07 V-08 V-09	708298 709299 710300

V-12	711 301
V-17	1364 459
V-18	712
V-20	713 302
V-24	714 303
V-25	1365 460
V-28	1189 405
V-35	1366 461
V-37	716
V-38	1190 406
V-39	1109 389
V-40	717 304
V-41	718 305
V-47	
	1368 463
V-48	719 306
V-49	1369 464
V-55	77499
V-57	720 307
V-58	1370 465
V-61	721 308
V-64	722 309
V-65	723
V-68	1448 484
V-71	
	1495 496
V-74	724 310
V-75	1372 467
	726 311
V-80	
V-81	727 <u>312</u>
V-87	728 313
V-90	1374 468
VI-02	340
VI-03	341
VI-04	342
VI-06	343
VI-07	344
VI-08	345
VI-09	346
VI-11	347
	0.000.41
VT-12	
VI-12	869 341
VI-13	870 342
VI-13 VI-14	870 342 871 343
VI-13 VI-14 VI-16	870342 871343 873344
VI-13 VI-14 VI-16 VI-18	870342 871343 873344 348
VI-13 VI-14 VI-16	870342 871343 873344
VI-13 VI-14 VI-16 VI-18 VI-19	870342 871343 873344 348 349
VI-13 VI-14 VI-16 VI-18 VI-19 VI-20	870342 871343 873344 348 349 350
VI-13 VI-14 VI-16 VI-18 VI-19 VI-20 VI-21	870342 871343 873344 348 349 350 351
VI-13 VI-14 VI-16 VI-18 VI-19 VI-20	870342 871343 873344 348 349 350
VI-13 VI-14 VI-16 VI-18 VI-19 VI-20 VI-21	870342 871343 873344 348 349 350 351
VI-13 VI-14 VI-16 VI-18 VI-19 VI-21 VI-22 VI-23	870342 871343 873344 348 349 350 351 352 878347
VI-13 VI-14 VI-16 VI-18 VI-19 VI-20 VI-21 VI-22 VI-23 VI-24	870342 871343 873344 348 349 350 351 351 352 878347 879348
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VI-93	1391 475
VI-95	915 374
VI-96	1392 476
VII-02	547
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VII-04	549
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VII-19	562 171
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VII-21	564 173
VII-22	565 174
VII-23	566 175
VII-24	567 176
VII-25	1397 480
VII-26	250 5
VII-27	568 177
	569
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VII-29	570 178
VII-32	571 179
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VII-36	575 182
VII-39	576 183
VII-40	577 184
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VII-52	587 193
VII-53	588 194
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VII-58	592 198
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VII-62	594 200
VII-63	595 201
VII-64	596 202
VII-65	597 203
VII-66	598 204
VII-67	1399 481
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VII-72	600206
VII-73	601 207
VII-74	602 208
VII-76	603 209
VII-77	604
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XI-13		
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XI-67		
XII-07		
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XII-07	XI-81	
XII-36		1213 427
XII-36	XII-35	1214 428
XII-65		1215 429
XII-65	XII-59	1216 430
XIII-03		1028 381
XIII-03		1217 431
XIII-04		
XIII-19		1218 432
XIII-24		1219 433
XIII-52		926 376
XIII-52	XIII-51	938 377
XIII-67	XIII-52	939 378
XIII-88	XIII-67	
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XVII-A2 II/S 2A6		
	VATT-A2	11/2390

Note

Sequences not available for sequence IDs in Table 1, and corresponding sequence Ids in Table 2 and 4.

298, 301, 305, 307, 312, 317, 318, 319, 320, 332, 333, 334, 336, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 367, 372, 375, 376, 377, 379, 385, 392, 393, 404, 437, 439, 440, 443, 444, 445, 449, 455, 457, 465, 466, 467, 468, 470, 486, 498, 501, 511, 514, 516, 517, 520, 522, 528, 531, 535, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 573, 584, 604, 608, 616, 620, 623, 640, 659, 662, 664, 667, 668, 673, 677, 678, 679, 681, 695, 702,

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Table 2a

List of informative probes for diagnosis of breast cancer

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Clone	Sequence
ID	ID SEQ ID
	NO. in
	Sequence
I-24	Listing
	308 11
I-28	310 13
I-30	1180 398
I-52	_
I-54	1181 399
II-41	397 60
II-70	424 86
II-87	441 100
III-06	458 109
III-20	1183 401
III-40	488 132
III-57	504 145
III-60	
III-61	507 148
	530 165
III-89	
IV-14	684 275
IV-15	1185 402
IV-26	1186 403
IV-32	688 279
IV-11	_
IV-53	61 498
IV-62	_
IV-69	192 4
IV-80	192 4 701 291
IV-82	196
IX-10	736 314
IX-12	-
IX-38	757 317
IX-39	758
IX-12	_
IX-48	764 319
IX-77	785 325
V-11	1188404
V-32	_
V-39	_
V-55	77 499
V-80	726 311
V-94	_
VI-07	93 1
VI-34	
VI-41	
	201355
VI-48	891 355
VI-49 VI-52	
VI-52 VI-55	- 897 359
	89/ 359
VI-65	-
VI-70	108 2

Clone ID	Comiondo
CTOUG ID	Sequence
	HDSEQ ID
	NO. in
	Sequence_
_	Listing
VI-72	-
VI-78	-
VI-84	-
VII-03	1196 411
VII-15	1199 414
VII-32	571 179
VII-39	576 183
VII-47	1200 415
VII-48	1201 416
VII-60	-
VII-73	601 207
V <u>II-77</u>	1203 418
VII-90	612 216
VIII-20	628 229
VIII-29	635 236
VIII-30	636 237
VIII-31	637 238
VIII-39	_
VIII-44	-
VIII-46	649 249
VIII-48	651 251
VIII-66	665 262
VIII-74	-
VIII-76	675 270
X-04	_
X-07	808 328
X-15	814 329
X-29	821 331
X-34	_
X-35	-
	- 837 334
X-56	839 335
X-68	1207 421
X-72	849 336
X-94	860 337
XI-07	-
XI-13	1209 423
XI-50	
XI-58	 _
XI-81	- 1212 426
	1212 426 1213 427
XII-07	1213 42/
XII-17	-
XII-26	-
XII-27	_
XII-31	-
XII-32	-
XII-35	1214 428

Clone ID	Sequence ID
XII-36	_
XII-52	_
XII-59	1216 430
XIII-19	1219 433
XIII-29	_
XIII-52	939 378
XIII-62	_
XIII-84	_
XIII-92	1221 435
XV-18	-
XV-22	1099 388
XV-24	-
XV-25	1224 436
XV-28	-
XV-34	-
XV-12	-
XV-68	_
XV-74	1
XV-93	-
XV-94	-
XV-96	-
XVI-36	1056 382
XVI-53	1230 439
XVI-59	-
XVI-66	1074 384
XVI-76	1083 386
XVI-77	1084 387
XVII-07	-
XVII-08	-
XVII-17	-
XVII-28	-
XVII-29	1120200
XVII-31	1139 392
XVII-36	_
XVII-39	1001440
XVII-40	1231 440
XVII-48 XVII-55	1148 393
XVII-58	_
	_
XVII-67 XVII-72	_
XVII-76	1160 394
XVII-76 XVII-82	1100 394
	1165 395
XVII-87 XVII-95	1172 396
VATT-20	1172 330

Table 2b

List of sequences of probes informative for breast cancer

Please see the note at the bottom of Table 1. Some sequences are missing.

Clone ID	Sequence IDSEQ ID NO. in Sequence Listing
I-13	1331 444
I-14	1178 397
I-24	308 11
I-25	309 12
I-28	310 13
I-30	1180 398
I-37	1440 482
I-42	1332 445
I-48	321 19
I-54	1181 399
I-60	327 25
I-72	1335 446
I-81	338 31
I-82	339 32
I-86	1336 447
I-88	1182 400
I-95	1337 448
II-02	360 33
II-03	361 34
II-06	364 36
II-07	365 37
II-10	368 39
II-21	378 45
II-23	380 46
II-24	381 47
II-25	382 48
II-27	384 50
II-33	390 55
II-34	391 56
II-41	397 60
II-42	398 61
II-46	401 64
II-47	1338 449
II-48	403 66

TT_52	406 68
II-52	40000
II-57	411 73
II-58	412 74
II-59	413 75
II-60	414 76
II-61	415 77
II-62	416 78
II-64	418 80
II-67	421 83
II-69	423 85
II-70	424 86
II-74	428 90
II-80	43496
II-82	
II-84	
II-87	
II-88	442 101
II-96	450 105
III-01	452 106
III-02	453 107
III-06	458 109
III-08	460 111
III-12	463 114
III-13	164 115
III-17	1344 450
III-18	469 116
III-20	1183 401
III-21	471 117
III-23	473 119
III-24	474 120
III-25	475 121
III-26	476 122
III-27	477 <u>123</u>
III-28	478 124
III-29	479 125
III-32	482 127
III-33	483 128
III-35	485 130
III-39	487 131
III-40	488 132
III-42	489 133
III-45	492 135
III-46	493 136
III-47	494 <u>137</u>
III-48	495 <u>138</u>
III-56	503 <u>144</u>
III-57	504 <u>145</u>

III-58	505 146
III-59	506 147
III-61	507 148
III-62	508 149
III-63	509 150
III-64	510 151
III-66	512 152
III-67	513 153
III-70	515 154
III-74	 518 155
III-75	519 156
III-78	 521 157
III-80	 523 158
III-81	524 159
III-82	1348 451
III-85	526 161
III-86	527 162
III-88	527 162 529 163 + 164
III-89	530 165
III-89	1351 452
III-93	532 166
III-95	534 168
III-96	1352 452
IV-04	682 273
IV-13	683 274
IV-14	684 275
IV-15	1185 402
IV-17	685 276
IV-23	1353 454
IV-26	1186 403
IV-31	687 <u>278</u>
IV-32	688 279
IV-35	1355 455
IV-37	G6 497
IV-38	689 280
IV-42	691 282
IV-43	1239 441
IV-47	693 284
IV-53	61 498
IV-61	696 286
IV-64	697 287
IV-69	192 4
IV-72	699 289
IV-80	701 291
IV-82	196
IV-85	702 292
IV-93	1360 457
IV-96	705 295

IX-10	736 314
IX-12	738
IX-13	739 315
IX-24	747 316
IX-38	757 317
IX-39	758 318
IX-48	764 319
IX-50	766 320
IX-56	768 321
IX-62	773 322
IX-65	776 323
IX-72	782 324
IX-77	785 325
IX-91	796 326
IX-96	801 327
V-01	1361 458
V-03	706 296
V-04	707 297
V-07	708 298
V-08	709 299
V-11	1188 404
V-12	711 301
V-17	1364 459
V-24	714 303
V-25	1365 460
V-28	1189 405
V-38	1366 461
V-38	1190 406
V-39	1109 389
V-41	718 <u>305</u>
V-47	1368 463
V-49	1369 464
V-55	77 499
V-57	720 307
V-58	1370 465
V-61	721 308
V-64	722 309
V-65	1371466
V-68	1448484
V-71	1495 496
V-74	724 310
V-75	1372 467
V-80	726 311
V-90	1374 468
VI-03	864 <u>338</u>
VI-04	865 339
VI-07	93 1
VI-08	867 340

VI-12 {	1378 469 369 341
1 11 10	370 342
VI-14 €	371 343
	373 344
	375 345
	376 346
	380 470
	378 347
	379 348
	192408
	381 349
	385 <u>351</u>
	387 352
	382 471
	1302 <u>471</u> 1193409
	389 353
	391 355
	392 501
	393 356
	395 357
	397 359
	399 361
	903 363
	304 364
	 L08 2
VI-71 4	
	
VI-75 4	 306 366
VI-76	207 367
VI-77 1	
VI-79 4	1389 473
AI-80	208 368
VI-85	310 369
VI-87	911 370
AI-88)12 371
VI-90 4	-390 474
VI-93 4	1391 475
VI-95)15 374
VI-96 4	1392 476
VII-02 4	1195 410
VII-03	.196 411
VII-06	1394 477
	197 412
VII-09	198 413
VII-10	<u> 1395</u> 478
	1396 479
VII-15 4	1199 414

VII-17	560 169
VII-19	562 171
VII-21	564 173
VII-22	565 174
VII-23	566 175
VII-24	567 176
VII-25	1397 480
VII-26	
VII-27	568 177
VII-29	570 178
VII-32	571 179
VII-33	575 180
VII-36	575 182
VII-39	576 183
VII-41	578 185
VII-42	579 186
VII-43	580 187
VII-46	583 190
VII-47	1200 415
VII-48	1201 416
VII-49	585 <u>191</u>
VII-54	589 195
VII-57	591 197
VII-58	592 198
VII-59	593 199
VII-62	594 200
VII-63	1202 417
VII-64	596 202
VII-66	598 204
VII-67	1399 481
VII-72	600 206
VII-73	601 207
VII-77	1203418
VII-80	605 210
VII-82	607212
VII-86	1453 487
VII-87	610 214
VII-90	
VII-91	 613 217
VII-92	
VII-93	615 219
VII-96	617 220
VIII-09	618221
VIII-10	619222
VIII-10	622 224
VIII-16	624 225
VIII-16 VIII-20	628 229
VIII-21	629 230

VIII-22	1455
VIII-23	630 231
VIII-24	631 232
VIII-25	632 233
VIII-26	1456 489
VIII-27	633234
VIII-28	634235
VIII-29	635 236
VIII-30	636 237
VIII-31	637 238
VIII-32	638 239
VIII-33	639 240
VIII-34	1204 419
VIII-38	643 243
VIII-40	644 244
VIII-41	645 245
VIII-46	649 249
VIII-48	651 251
VIII-55	656 256
VIII-57	658 258
VIII-59	660 _ <u>259</u>
VIII-60	661 260
VIII-61	1205 420
VIII-64	663 261
VIII-66	665 262
VIII-73	672 267
VIII-74	673 268
VIII-76	675 270
VIII-80	679 272
X-07	808 328
X-15	814 329
X-20	817 330
X-29	821 331
X-34	825 332
X-46	833 333
X-54	837 334
X-56	839 335
X-68	
X-72	849 336
X-73	1208 422
X-94	860 337
XI-13	1209 423
XI-37	1460490
XI-43	1210 424
XI-43	1210 425
XI-87 XI-81	1212 425
	1212 426 1213 427
XII-07 XII-35	1213 427
V11-22	1211 120

XII-36	1215 429
XII-59	1216 430
XII-65	1028 <u>381</u>
XII-92	1217 431
XIII-03	917 375
XIII-04	1218 432
XIII-19	1219 433
XIII-24	926 376
XIII-51	938 377
XIII-52	939 378
XIII-67	947 <u>379</u>
XIII-69	949 380
XIII-88	1220 434
XIII-92	1221 435
XV-22	1099 388
XV-24	1101
XV-25	12224 436
XV-12	1108
XV-62	1226 437
XV-64	1118 390
XV-84	1125 391
XVI-19	1228 438
XVI-36	1056 382
XVI-53	1230 439
XVI-60	1071 383
XVI-66	1074 384
XVI-74	1081 385
XVI-76	1083 386
XVI-77	1084 387
XVII-31	1139 392
XVII-40	1231 440
XVII-48	1148 393
XVII-76	1160 394
XVII-87	1165 395
XVII-95	1172 396

Table 3

List of informative probes (Clone ID) selected for breast cancer diagnosis based on their occurrence criterion during variable selection

Occurrence*	Clone ID
100%	XI-8,XVI-66,VIII-66,XVI-59,VII-03,XIII-19,XII-35,X-35,XI-50,XII-26,IV-53,XIII-29,XIII-62,I-30,III-06,XV-22,XV-94,VII-15,VII-39,IX-39,XVII-39,III-40,VII-32
90%	1-52,VI-65,VI-34,IV-62,XV-34,XVII-58, V-11, VI-78,XII-36, XIII- 92,VIII-29,XVI-53,XVI-77,XI-13, XIII-84, IV-14, XII-31, V-80,VII- 48, XVII-29,XVII-72
80%	III-60,VIII-74,IX-12,X-04, XIII-52,VIII-30,IX-38
70%	VI-49, X-29,VIII-48
60%	IV-82, IX-10, VI-52, X-68,VII-77
50%	IV-15
40%	XV-28, II-70,V-55
30%	XVII-17,XVII-67
20%	XI_58, XVI_36, VIII_39,VIII_44, III_61,IV_69, XV_68, X_72
10%	IX-42, IX-77,X-94 ,XV-96,XVII-55
5%	XII-59,XVI-76,I-54, XV-18,V-94, X-54,VI-07,VII-47,XVII-31,XVII-87,XVII-48
In at least one model	II-41, VI-41, III-57, III-89, VII-73, XV-25, IV-26, X-34, IV-41, VII-90, XV-42, XVII-82, XII-27, VIII-20, I-28, VII-60, VIII-76, III-20, VI-84, XI-07, XVII-28, XII-17, XVII-36, XII-52, X VII-76, VIII-46, VI-70, XV-74, XV-93, VIII-31, II-87, V-39, VI-55, X-07, X-15, XII-07, XVII-07, XVII-08, XVII-95, I-24, IV-32, V-32, VI-48, VI-72, IV-80, IX-48, X-56, XV-24, XII-32, XVII-40

^{*100%} = Genes appearing in all the 75 cross validated models; 90% = Additional genes appearing in at least 68 out of 75 cross validated models; 5% = Additional genes appearing in at least 4 out of 75 cross validated models and so on.

Clone	Sequence
ID	ID SEQ ID
	NO. in
	Sequence
	Listing
I-01	_
I-02	_
	_
I-13	_
I-21	_
I-34	313 15
I-37	_
T-12	_
I-58	22624
	326 24
I-71	-
I-72	-
I-86	_
T-95	_
2 20	26124
II-03	361 34
II-05	363 35
II-06	364 36
II-10	368 39
II-24	381 47
	382 48
II-26	383 49
II-33	390 55
II-34	39 56
II-42	398 61
	37001
	-
II-57	411 73
II-61	415 77
II-69	123 85
II-75	429 91
II-83	-
II-84	438 99
II-88	442 101
	112101
II-90	_
II-94	448 104
III-02	453 107
III-05	
111 00	
III-06	458 <u>109</u>
III-08	460 111
III-10	_
	16111
III-13	464 <u>115</u>
III-15	_
III-17	_
III-23	473 119
	476 122
III-26	
III-35	485 130
III-39	487 131
III-43	490 500
III-44	491 134
III-53	500 142
III-56	503 144

Clone ID	Sequence IDSEQ ID NO. in Sequence Listing
III-60	HISCHING
	_
III-63	509 150
III-68	_
III-74	518 155
III-80	523 158
III-82	_
III-85	526 161
III-92	_
III-96	_
IV-23	_
IV-29	-
IV-31	687 278
IV-34	-
IV-35	-
IV-45	_
IV-80	701 291
IV-82	_
IV-93	
77 01	_
V-02	
V-03	706006
	706 296
V-04	707 297
V-06	-
V-07	708 298
V-12	711 301
V-15	_
V-17	_
V-21	_
V-25	_
V-35	_
V-42	
V-43	
	-
V-17	-
V-49	-
V-52	-
V-54	_
V-58	-
V-59	-
V-65	_
V-68	_
V-71	_
V-75	_
V-79	_
V-80	726 311
V-90	720 <u>211</u>
V-91	-
V-92	_

Clone	Sequence
ID	ID SEQ ID
	NO. in
	Sequence
0.0	Listing
VI-02	-
VI-04	865 339
VI-09	_
VI-10	_
VI-12	869 341
VI-14	871 343
VI-17	_
VI-20	876 346
VI-21	_
VI-23	878 347
VI-41	070317
	-
VI-42	_
VI-43	_
VI-44	_
VI-48	891 355
VI 40	
	000055
VI-50	893 356
VI-53	895 357
VI−71	_
VI-74	905 365
VI-76	907 367
	307307
VI-78	_
VI-79	-
VI-87	911 370
VI-88	912 371
	712 371
VI-90	_
VI-93	_
VI-95	915 374
VI-96	1 2 1 3 2 / 1
	_
VII-02	
V I I U Z	-
VII-03	-
VII-03	-
VII-03 VII-06	-
VII-03 VII-06 VII-10	-
VII-03 VII-06	- - -
VII-03 VII-06 VII-10 VII-11	- - - - - - - - - - - - - - -
VII-03 VII-06 VII-10 VII-11 VII-19	- - - - - 563171
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21	- - - - - - - - 563 <u>171</u> 564 <u>173</u>
VII-03 VII-06 VII-10 VII-11 VII-19	
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21	
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36	564 <u>173</u> - 575 <u>182</u>
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42	564173 - 575182 879186
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43	564173 - 575182 879186 580187
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42	564173 - 575182 879186
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46	564 <u>173</u> - 575 <u>182</u> 879 <u>186</u> 580 <u>187</u> 583 <u>1</u> 90
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59	564173 - 575182 879186 580187 583190 593199
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63	564173 - 575182 879186 580187 583190 593199 595201
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59	564173 - 575182 879186 580187 583190 593199
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66	564173 - 575182 879186 580187 583190 593199 595201
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-66	564173 - 575182 879186 580187 583190 593199 595201 598204
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73	564173 - 575182 879186 580187 583190 593199 595201 598204
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206
VII-03 VII-06 VII-10 VII-11 VII-19 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-75	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207
VII-03 VII-06 VII-10 VII-11 VII-19 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-73 VII-75 VII-02 VII-04	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-02 VI-04 VI-09	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-02 VI-04 VI-09	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207
VII-03 VII-06 VII-10 VII-11 VII-19 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-75 VII-02 VII-09 VII-09	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207 - 866
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-75 VII-02 VII-09 VII-10 VII-12	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207 - 866 - 873344
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-63 VII-66 VII-67 VII-72 VII-73 VII-73 VII-75 VII-02 VII-09 VI-10 VI-12 VI-14	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207 - 866
VII-03 VII-06 VII-10 VII-11 VII-19 VII-21 VII-25 VII-36 VII-42 VII-43 VII-46 VII-59 VII-63 VII-66 VII-67 VII-72 VII-73 VII-75 VII-75 VII-02 VII-09 VII-10 VII-12	564173 - 575182 879186 580187 583190 593199 595201 598204 - 600206 601207 - 866 - 873344

	~
Clone ID	Sequence
	ID SEQ ID
	NO. in
	Sequence
77TT 01	Listing 613 217
VII-91	
VII-93	615 219
VIII-01	_
VIII-02	_
VIII-03	_
VIII-06	_
VIII-09	618 221
	010 ZZ1
VIII-10	-
VIII-15	_
VIII-22	_
VIII-26	_
VIII-28	634 235
VIII-30	636 237
VIII-32	638 239
VIII-33	639 240
VIII-41	645 245
VIII-42	646 246
VIII-48	651 251
VIII-58	_
VIII-64	663 261
VIII-65	~~~ ∠∪⊥
	-
VIII-67	666 263
VIII-78	_
VIII-82	_
VIII-83	
	1
VIII-85	-
VIII-87	_
VIII-91	
VIII-92	
	_
VIII-93	1
VIII-95	-
-	

Table 4b

List of sequences of probes informative for Alzheimer disease

Please see note to Table 1

Clone ID	Sequence IDSEQ ID NO. in
I-09	Sequence Listing
I-10	299 6
I-15	300 7
I-16	-
I-17	302 8
I-19	304 9
I-20	305
I-22	306 10
1-23	307
I-24	308 11
I-25	309 12
I-28	310 13
I-31	311 14
I-32	312
I-34	313 15
I-38	314 16
I-39	315 17
I-40	316 18
I-44	317
I-15	318
I-16	319
I-17	320
I-48	321 19
I-49	322 20
I-53	323 21
I-56	324 <u>22</u>
I-57	325 23
I-58	326 24
I-60	327 25
I-64	328 26
I-67	330 27
I-69	331 28
I-71	332
1-72 1-73	333
	334
I-77	335 <u>29</u> 336
I-80	
I-80	337 30 338 31
I-81	339 32
VI-02	339 32 340
VI-03	341
VI-04	342
VI 07	□ 1 Z

VI-06	343
VI-07	344
VI-08	345
VI-09	346
VI-11	347
VI-18	348
VI-19	349
VI-20	350
VI-21	351
VI-22	352
VI-25	353
VI-26	354
VI-27	355
VI-31	356
VI-33	357
VI-35	358
VI-18	359
	360 33
II-02	_
II-03	361 <u>34</u>
II-05	363 <u>35</u>
II-06	364 36
II-07	365 37
II-08	366 38
11-09	
II-10	368 39
	369 40
II-11	309 40
	07044
II-12	370 41
II-13	371 42
	371 42 372
II-13	371 42
II-13 II-14	371 42 372
II-13 II-14 II-15	371 <u>42</u> 372 373 <u>43</u>
II-13 II-14 II-15 II-16	37142 372 37343 37444
II-13 II-14 II-15 II-16 II-17 II-18	37142 372 37343 37444 375
II-13 II-14 II-15 II-16 II-17 II-18 II-20	37142 372 37343 37444 375 376
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21	37142 372 37343 37444 375 376 377 37845
II-13 HI-14 II-15 II-16 HI-17 HI-18 HI-20 II-21 HI-22	37142 372 37343 37444 375 376 377 37845 379
II-13 HI-14 II-15 II-16 HI-17 HI-18 HI-20 II-21 HI-22 II-23	37142 372 37343 37444 375 376 377 37845 379
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-21 II-22 II-23 II-24	37142 372 37343 37444 375 376 377 37845 379 38046 38147
II-13 HI-14 II-15 II-16 HI-17 HI-18 HI-20 II-21 HI-22 II-23	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26	37142 372 37343 37444 375 376 377 37845 379 38046 38147
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-23 II-23 II-24 II-25 II-25 II-26 II-27 II-28	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27 II-28 II-29 II-30	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-23 II-24 II-25 II-25 II-26 II-27 II-28 II-29 II-30 II-31	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-23 II-24 II-25 II-25 II-26 II-27 II-28 II-29 II-30 II-31 II-32	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27 II-28 II-29 II-30 II-31 II-32 II-33	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954 39055
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27 II-29 II-30 II-31 II-32 II-33 II-34	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954 390555 39156
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27 II-28 II-30 II-30 II-31 II-32 II-34 II-34 II-35	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954 39055 39156 392
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-23 II-24 II-25 II-25 II-26 II-27 II-28 II-29 II-30 II-31 II-32 II-33 II-34 II-35 II-37	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954 39055 39156 392
II-13 II-14 II-15 II-16 II-17 II-18 II-20 II-21 II-22 II-23 II-24 II-25 II-26 II-27 II-28 II-30 II-30 II-31 II-32 II-34 II-34 II-35	37142 372 37343 37444 375 376 377 37845 379 38046 38147 38248 38349 38450 385 38651 38752 38853 38954 39055 39156 392

II-39	395 58
II-40	396 59
II-41	397 <u>60</u>
II-42	398 <u>61</u>
II-43	399 62
II-44	400 63
II-46	401 64
II-47	402 65
II-48	403 66
II-49	
II-50	405 67
II-52	
II-53	
II-54	
II-55	
II-56	
II-57	
II-58	
II - 59	
II-60	
II-61	415 77
II-62	116 78
II-63	417 79
II-64	418 80
II-65	41981
II-66	42082
II-67	120 <u>02</u> 121 83
II-68	121<u>00</u> 122 84
II-69	122 01 123 85
II-70	123<u>05</u> 424 86
II-71	121<u>8</u> 425 87
II-72	123<u>07</u> 126 88
II-73	127 89
II-74	42890
II-75	429 91
II-76	43092
II-77	431 93
II-78	432 94
II-79	433 95
II-80	434 96
II-81	435 97
II-82	436 98
II-83	437
II-84	438 99
11-85	439
11-86	440
II-87	441 100
II-88	442101
11-89	443
11-03	444
II-90 II-91	445
11 71	770

II-92	446 102
II-93	447 103
II-94	448 104
II-95	449
II-96	450 105
III-01	452 106
III-02	
III-03	454 108
III-04	
III-05	457
III-06	458 109
III-07	459 110
III-08	
III-09	461 112
III-11	462 113
III-12	463 114
III-13	464 115
III-14	<u>——</u> 465
III-15	466
III-16	467
III-17	468
III-18	469
III-19	470
III-21	471 117
III-22	472 118
III-23	473 119
III-24	474 120
III-25	
III-26	476 122
III-27	477 123
III-28	478 124
III-29	479 125
III-31	481 126
III-32	482 127
III-33	483 128
III-34	484 129
III-35	485 130
III-37	486
III-39	487 131
III-40	488 132
III-42	489 133
III-43	490 500
III-44	491 134
III-45	492 135
III-46	493 136
III-47	494 137
III-48	495 138
III-49	496 139
III-50	497 140
III-51	498
III-52	499 <u>141</u>

III-53	HII-54 III-55 III-56 III-57 III-58 III-59 III-61 III-62 III-63 III-64 HII-65 III-66 III-67 HII-69 III-70 HII-71 HII-73 III-74 III-75 HII-75 HII-75 HII-75 HII-75 HII-75 HII-77 III-78 HII-79
III-55 502143	III-55 III-56 III-57 III-58 III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
III-56	III-56 III-57 III-58 III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-70 III-70 III-71 III-72 III-74 III-75 III-75 III-75 III-78 III-78
III-56	III-56 III-57 III-58 III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-70 III-70 III-71 III-72 III-74 III-75 III-75 III-75 III-78 III-78
III-57 \$04145 III-58 \$05146 III-59 \$06147 III-61 \$07148 III-62 \$08149 III-63 \$09150 III-64 \$10151 III-65 \$11 III-67 \$13153 III-69 \$14 III-70 \$15154 III-71 \$16 III-72 \$18155 III-73 \$17 III-74 \$18155 III-75 \$19156 III-77 \$20 III-78 \$2157 III-79 \$22 III-80 \$23158 III-81 \$24159 III-83 \$25160 III-85 \$26161 III-87 \$28	III-57 III-58 III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
III-58	III-58 III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
III-59 S06147 III-61 S07148 III-62 S08149 III-63 S09150 III-64 S10151 S11-65 S11 III-66 S12152 III-67 S13153 S14 III-70 S15154 III-70 S15154 III-71 S16 S17 III-74 S18155 III-75 S19156 III-75 S19156 III-75 S20 III-78 S22 III-80 S23158 III-81 S24159 III-83 S25160 III-85 S26161 III-86 S27152 III-86 S27152 III-87 S28 III-87 III-87 S28 III-87 S28 III-87 III-87 S28 III-87 III-	III-59 III-61 III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-74 III-75 III-75 III-75 III-77 III-78 III-78
III-61	III-61 III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-75 III-77 III-78 III-78
TIII-62 \$508149 TIII-63 \$509150 TIII-64 \$510151 TIII-65 \$511 TIII-66 \$512152 TIII-67 \$513153 TIII-69 \$514 TIII-70 \$515154 TIII-71 \$516 TIII-73 \$517 TIII-74 \$518155 TIII-75 \$519156 TIII-77 \$520 TIII-78 \$521157 TIII-79 \$522 TIII-80 \$523158 TIII-81 \$524159 TIII-83 \$525160 TIII-85 \$526161 TIII-87 \$528 TIII-87	III-62 III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-73 III-74 III-75 III-78 III-78
III-63	III-63 III-64 III-65 III-66 III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-78
III-64	III-64 III-65 III-66 III-67 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-78
TII	HII-65 III-66 III-67 HII-69 III-70 HII-73 III-74 III-75 HII-77 III-78 HII-79
III-66	III-66 III-67 III-69 III-70 III-73 III-74 III-75 III-77 III-78 III-78
III-67	III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
III-67	III-67 III-69 III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
TII	HII-69 III-70 HII-71 HII-73 III-74 III-75 HII-77 III-78 HII-79
III-70 \$15154 III-71 \$16 III-73 \$17 III-74 \$18155 III-75 \$19156 III-77 \$20 III-78 \$21157 III-79 \$22 III-80 \$23158 III-81 \$24159 III-83 \$25160 III-85 \$26161 III-86 \$27152 III-87 \$28	III-70 III-71 III-73 III-74 III-75 III-77 III-78 III-79
### Til 71	HII-71 HII-73 III-74 III-75 HII-77 III-78 HII-79
III - 73 517 III - 74 518155 III - 75 519156 III - 77 520 III - 78 521157 III - 79 522 III - 80 523158 III - 81 524159 III - 83 525160 III - 85 526161 III - 86 527152 III - 87 528	HII-73 III-74 III-75 HII-77 III-78 HII-79
III-74 518155 III-75 519156 III-77 520 III-78 521157 III-80 523158 III-81 524159 III-83 525160 III-85 526161 III-86 527152 III-87 528	III-74 III-75 III-77 III-78
III-75	III-75 III-77 III-78 III-79
III-77 520 III-78 521157 III-79 522 III-80 523158 III-81 524159 III-83 525160 III-85 526161 III-86 527152 III-87 528	III-77 III-78 III-79
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III-79 522 III-80 523158 III-81 524159 III-83 525160 III-85 526161 III-86 527152 III-87 528	III-79
III-80 523158 III-81 524159 III-83 525160 III-85 526161 III-86 527152 III-87 528	
III-81	III-80
III-83	
III-85 526161 III-86 527152 III-87 528	III-81
III-86 <u>527</u> 152 <u>III-87</u> <u>528</u>	III-83
III-86 <u>527</u> 152 <u>III-87</u> <u>528</u>	III-85
III-87 528	
5/4 63/ 64	III-88
III-89 530 165	
III-91 531	
III-93 <u>532</u> 166	
III-94 <u>533</u> 167	
III-95 <u>534</u> 168	
III-96 535	
VII-02 547	
VII-03 548	VII-03
VII-04 549	VII- 04
VII-05 550	
VII-06 551	VII-06
VII-07 552	VII-07
VII-08 553	VII-08
VII-09 554	VII-09
VII-10 555	
VII-11 556	
VII-12 557	
VII 12 557 VII 14 558	
VII-15 559	
	V II I I I
	T/TT 17
VII-18 <u>561</u> 170	VII-17

VII-19	562 171
VII-20	563 172
VII-21	564 173
VII-22	565 174
VII-23	566 175
VII-24	567 176
VII-27	 568 177
VII-28	
VII-29	570 178
VII-32	571 179
VII-33	572 180
VII-34	573
VII-35	574 181
VII-36	575 182
VII-39	576 183
VII-40	577 <u>184</u>
VII-41	578 185
VII-42	579 186
VII-43	580 <u>187</u>
VII-44	581 188
VII-45	582 189
VII-46	583 190
VII-48	584
VII-49	585 191
VII-50	586 192
VII-52	587 193
VII-53	588 194
VII-54	589 195
VII-55	590 196
VII-57	591 197
VII-58	592 198
VII-59	 593 199
VII-62	
VII-63	
VII-64	596 202
VII-65	597 203
VII-66	598 204
VII-71	599 205
VII-71 VII-72	600 206
VII-72 VII-73	601 207
VII-74	602208
VII-76	603209
VII-77	604
VII-80	605 210
VII-81	606 211
VII-82	607 212
VII-83	608
VII-84	609213
VII-87	610 214
VII-89	611 215
VII-90	612 216

VII-91	613 217
VII-92	614 218
VII-93	615 219
VII-94	616
VII-96	617 220
VIII-09	618 221
VII-10	619 222
VII-11	
VII-12	621 223
VII-13	622 224
VII-15	623
VII-16	624 225
VII-17	625 226
VII-17 VII-18	626 227
VII-19	627228
VII-20	628229
VII-21	629230
VII-23	630 231
VII-24	631 232
VII-25	632 233
VII-28	634 235
VII-29	635 236
VII-30	636 237
VII-31	637 238
VII-32	638 239
VII-33	639 240
VII-34	640
VII-36	641 <u>241</u>
VII-37	612 242
VII-38	643 243
VII-40	644 <u>244</u>
VII-41	645 245
VII-42	646 246
VII-43	647 247
VII-45	648 248
VII-46	649 249
VII-47	650 250
VII-48	651 <u>251</u>
VII-50	652 252
VII-51	653 253
VII-53	654 254
VII-54	655 255
VII-55	656 256
VII-56	657 257
VII-57	658 258
VII-58	
VII-59	660 259
VII-60	661 260
VII-61	
VII-64	663 261
VII-65	664

VII-66	665 262
VII-67	666 263
VII-68	667
VII-69	668
VII-70	669 264
VII-71	670 265
VII-72	671 266
VII-73	672 267
VII-74	673 268
VII-75	674 269
VII-76	675 270
VII-77	676 271
VII-78	677
VII-79	678
VII-80	679 272
IV-02	681
IV-04	682 273
IV-13	683 274
IV-14	684 275
IV-17	685 276
IV-28	686 277
IV-31	687 278
IV-32	688 279
IV-38	689 280
IV-40	690 281
IV-42	691 282
IV-44	692 283
IV-47	693 284
IV-55	694 285
IV-56	695
IV-61	696 286
IV-64	697 287
IV-65	698 288
IV-72	699 289
IV-73	700 290
IV-80	701 291
IV-85	702 292
IV-93	703 293
IV-95	704 294
IV-96	705 295
V-03	706 296
V-04	707 297
V-07	708 298
V-08	709 299
V-09	710 300
V-12	711 301
V-18	712
V-20	713 302
V-24	714 303
V-37	716
V-40	717 304

V-41	718 305
V-48	719 306
V-57	720 307
V-61	721 308
V-64	 722 309
V-65	723
V-74	724 <u>310</u>
V-80	726 311
V-81	727 <u>312</u>
V-87	728 313
VI-13	870 342
VI-14	871 343
VI-16	873 344
VI-23	878 347
VI-24	879 348
VI-28	883 350
VI-32	885 351
VI-38	886
VI-39	887 <u>352</u>
VI-45	889 353
VI-46	890 354
VI-49	892 501
VI-50	893 356
VI-52	
VI-53	895 357
VI-54	 896 358
VI-55	897 359
VI-57	898 360
VI-57	899 361
VI-63	900 362
VI-65	902
VI-66	903 363
VI-67	904 364
VI-74	905 <u>365</u>
VI-75	906 366
VI-76	907 367
VI-80	908 368
VI-81	909
VI-85	910 369
VI-87	911 370
VI-88	912 371
VI-91	 913 372
VI-94	914373
VI-95	915 374
VI-95	915 374 916
1-13	
	1177
I-14	1178 397
I-30	1180 398
I-54	1181 399
I-88	1182 400

III-20	1183 401	
IV-15	1185 402	
IV-26	1186 403	
IV-62		
V-11	1188404	
IV-28	1189 405	
IV-38	1190 406	
IV-45		
VI-44	1193 409	
VII-47		
I-42	1332 445	
I-52	1333 1333	
I-86	1336 447	
I-95	1337 448	
III-10	1342	
III-60	1347	
III-82	1348 451	
	1313 451 1351 452	
III-92		
IV-23	1353454	
IV-34	1354	
IV-35	1355 455	
IV-11	1356	
IV-45	1357	
IV-82	1359 456	
V-01	1361 458	
V-02	1362	
V-06	1363	
V-17	1364 459	
V-25	1365 460	
V-35	1366 461	
V-42	1367 462	
V-47	1368 463	
V-49	1369 464	
V-58	1370 <u>465</u>	
V-75	1372 467	
V-79	1373	
V-90	1374 468	
V-91	1375	
V-94	1376	
VI-10	1379	
VI-41	1381	
VI-43	1382 471	
VI-71	1387 472	
VI-72	1388	
VI-79	1389 473	
VI-90	1390 474	
VI-93	1391 475	
VII-25	1397 480	
VII-60	1398	
VII-67	1399 481	
VIII-22		

VIII-26	1404
VIII-39	1405
VIII-44	1406
I-37	1440 482
V-32	1445
V-52	1447 483
V-68	1448 484
V-92	1449 485
VI-42	1450 486
VI-78	1452
VII-86	1453 487
VII-88	1454 488
IV-29	1490 491
V-15	1491 491
V-39	1492 493
V-54	1493 494
V-59	1494 495
V-71	1495 496

Table 5

Samples

Dampico		
Diagnosis	No. of women	
Normal/Benign	42*	
DCIS	3	
Invasive cancer	26	

^{*}From one woman, whole blood was collected at weeks 1,2,3,4,5 following menstruation. Hence, the number of unique normal/benign samples tested in the experiment is 75.

Information about women with breast cancer

Sample	AGE	Stage	Cancer type	Size hist. (mm)	Nodes
1	51	II	IDC	20	1/7
2	84	II	IDC	22	2/2
3	50	I	DCIS+ 1 IDC	>50 DCIS; 5 x 14	0/7
4	47	I	IDC	15	0
5	69	III	ILC g.2 + tubular adenocarcinoma	50 + 3	1 av 12 + 1 av 7
6	50	II	IDC	24	0
7	65	I	IDC	15	0
8	63	II	IDC	23	0
9	55	I	IDC + DCIS	4	0 av 1
10	52	0	DCIS + small colloid carcinoma foci	50 + 3	0
11	60	II	IDC	24	0
12	54	I	IDC	11	0
13		0	DCIS	20	0
14	49	0	DCIS	9	0
15	48	I	IDC	4	0
16	56	I	IDC	4	0
17	68	I	IDC	14	0
18	68	I	IDC	7	0
19	63	I	IDC	10	0
20	45	I	IDC	19	1
21	57	III	IDC	60	8/20

22	55	II	IDC/DCIS	35 + 55	0
23	71	I	IDC/extensive DCIS	8	0
24	56	I	IDC	9	?
25	66	II	IDC	26	0
26	66	I	IDC	15	?
27	61	I	IDC	9	?
28	?	?	?	?	?
29	65	I	IDC	11	0

Other diseases/conditions present in the women tested

Other diseases/conditions present in the women tested

Disease/condition
Diabetes
Asthma
Ulcerous colitis
Hemochromatose
Crohn's disease
Fibromyalgia
Psoraiasis
Atopic eczema
Rheumatism
Allergies

Prior history of cancer in the women tested

Cancer type	No. of women
Breast	3
Colon	2
Stomach	1
Skin	1

Table 6

Number of samples tested by double cross validation and success of the diagnostic test for breast cancer based on selected ionformative genes

Number of samples tested by double cross validation

Number of unique samples tested	75
Number of unique non cancer samples tested	46
Number of cancer samples tested	29

Success of the diagnostic test for breast cancer based on selected informative genes

Occurrence in percentage*	Number of informative probes	Specificity	Sensitivity	Accuracy	False Positive rate	False negative rate	Total error rate
100.00	23	84.78	75.86	81.33	15.22	24.14	18.67
90.00	44	91.30	79.31	86.67	8.70	20.69	13.33
80.00	51	86.96	79.31	84.00	13.04	20.69	16.00
70.00	54	89.13	75.86	84.00	10.87	24.14	16.00
60.00	58	89.13	75.86	84.00	10.87	24.14	16.00
50.00	59	89.13	75.86	84.00	10.87	24.14	16.00
40.00	63	89.13	75.86	84.00	10.87	24.14	16.00
30.00	66	86.96	75.86	82.67	13.04	24.14	17.33
20.00	74	89.13	75.86	84.00	10.87	24.14	16.00
10.00	79	89.13	75.86	84.00	10.87	24.14	16.00
5.00	90	86.96	79.31	84.00	13.04	20.69	16.00
1.33	139	84.78	72.41	80.00	15.22	27.59	20.00

^{*100% =} Genes appearing in all the 75 cross validated models; 90% = Genes appearing in at least 68 out of 75 cross validated models; 5% = Genes appearing in at least 4 out of 75 cross validated models; and so on.

Table 7

Double cross-validation and details of the success of the diagnostic test for Alzheimer disease based on the expression 182 informative genes

Validation Result

Total number of samples tested	14
Number of Alzhelmer's disease samples tested	7
Number of Alzhelmer's disease samples incorrectly predicted	1
Number of non-Alzhelmer's disease samples tested	7
Number of non-Alzhelmer's disease samples incorrectly predicted	0

Success of diagnostic test

Performance	Description	8
Accuracy	Percentage of the total number of predictions that were correct	92.9
Sensitivity	Percentage of positive cases that were correctly identified	85.7
Specificity	Percentage of negatives cases that were correctly predicted	100
False positive rate	Percentage of negatives cases that were incorrectly classified as positive	0.0
False negative rate	Percentage of positive cases that were incorrectly classified as negative	14.3
Total error rate	Percentage of the total cases incorrectly predicted	7.1

Table 8

Some relevant features of the blood donors. B, Female donors with breast cancer; N, Female donors with suspected mammogram but no breast cancer; IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ; na, not available nd, not determined; ++, no degradation of mRNA and no ribosomal contamination in the sample, +, no degradation of mRNA but ribosomal contamination in the sample.

		AGE	Cancer type/ breast abnormality	Size Hist.	mRNA Quality
1	B1	na	IDC	5	++
2	В2	49	DCIS	8	nd
3	В3	54	IDC	18	++
4	В4	59	IDC	12	+
5	В5	61	DCIS + micro invasive cancer	15+1.5	++
6	В6	55	IDC	12+17	nd
7	В6		IDC	12+17	nd
8	Nl	45	Fibroadenoma	-	nd
9	N2	52	na	-	+
10	N3	55	Cyst	-	++
11	N4	54	na	-	++
12	N 5	51	Benign ductal epithelium	-	nd
13	N6	57	Benign	-	nd

14	N7	50	na		++
15	N8	52	na	-	+

Table 9

List of sequences of probes informative for both alzheimer and breast cancer disease

Clone ID	Sequence IDSEQ ID NO. in
	Sequence Listing
I-24	308 11
I-25	309 12
I-28	310 13
I-48	321 19
I-60	327 25
I-72	333
I-81	338 <u>31</u>
I-82	339 32
II-02	360 <u>33</u>
II-03	361 <u>34</u>
II-06	364 <u>36</u>
II-07	365 <u>37</u>
II-10	368 39
II-21	678 45
II-23	680 46
II-24	381 47
II-25	382 48
II-27	384 50
II-33	390 55
II-34	391 56
II-41	397 60
II-42	398 61
II-46	401 <u>64</u>
II-47	402 65
II-48	403 66
II-52	406 68
II-57	411 73
II-58	
II-59	413 75
II-60	414 76
II-61	
II-62	
II-64	
II-67	
II-69	
II-70	424 86
II-74	128 90
II-80	434 96
II-82	436 98
II-84	43899
II-87	441100
II-88	442101
L	11Z101

III-02 4 III-06 4 III-08 4	52106 53107 58109 60111
III-06 4 III-08 4	58 <u>109</u> 60111
III-08 <u>4</u>	
TTT_12 4	63 114
111-12 +	
III-13 4	64 115
III-17 4	68
III-18 4	69 116
III-21 4	71 117
III-23 4	73 <u>119</u>
III-24 4	74 120
III-25 4	75 121
III-26 4	76 122
III-27 4	77 123
III-28 4	78 124
III-29 <u>4</u>	79 125
III-32 4	82 127
III-33 4	83 128
III-35 4	85 130
III-39 4	87 131
III-40 4	88 132
III-42 4	89 133
III-45 4	92 135
III-46 4	93 136
III-47 4	94 137
III-48 4	95 138
III-56 5	03 144
III-57 5	04 145
III-58 5	05 146
III-59 5	06 147
III-61 5	07 148
III-62 5	08 149
	09 150
III-64 5	10 151
	12 152
	13 153
III-70 5	15 154
	18 155
III-5 5	19 156
III-78 5	21 <u>157</u>
III-80 5	23 158
	24 <u>159</u>
	26 161
	27 162
	29 163/164
III-89 5	30 165

III-93	532 166
III-95	534 168
III-96	535
IV-04	682 273
IV-13	683 274
IV-14	 684 275
IV-17	685 276
IV-31	687 278
IV-32	688 279
IV-38	689 280
IV-42	691 282
IV-47	
IV-61	693284
	696 286
IV-64	697 287
IV-72	699 289
IV-80	701 291
IV-85	702 292
IV-93	703 293
IV-96	705 295
V-03	706 296
V-04	707 297
V-07	708 298
V-08	709 299
V-12	711 <u>301</u>
V-24	714 <u>303</u>
V-41	718 <u>305</u>
V-57	720 307
V-61	721 308
V-64	722 309
V−65	723
V-74	724 <u>310</u>
V-80	726 311
VI-03	341
VI-04	342
VI-07	344
VI-08	345
VI-09	346
VI-12	869 341
VI-14	871 343
VI-19	349
VI−20	350
VI-21	351
VI-23	878 347
VI-25	353
VI-26	354
VI-48	359
VI-50	893 356

VI-53	895 357
VI-74	905 365
VI-76	907 367
VI-87	911 370
VI-88	912 371
VI-95	915 374
VII-02	547
VII-03	548
VII-06	551
VII-08	553
VII-08	554
VII-10	555
VII-11	556
VII-15	559
VII-17	560
VII-19	562 171
VII-21	
VII-22	
VII-23	 566 175
VII-24	567 176
VII-27	
VII-29	570 178
VII-32	571 179
VII-33	572 180
VII-36	575 182
VII-28	576 183
VII-41	 578 185
VII-42	579 186
VII-43	580 187
VII-46	583 190
VII-48	584
VII-49	585 191
VII-54	589 195
VII-57	591 197
VII-58	592 198
VII-59	593 199
VII-62	594 200
VII-63	595 201
VII-64	596 202
VII-66	598 204
VII-72	600 206
VII-73	601 207
VII-77	604
VII-80	605 210
VII-82	607 212
VII-87	610 214
VII-90	

VII-91	613 217
VII-92	614 218
VII-93	615 219
VII-96	617 220
VIII-09	618 221
VIII-10	619 222
VIII-13	622 224
VIII-16	624 225
VIII-20	628 229
VIII-21	629 230
VIII-23	630 231
VIII-24	631 232
VIII-25	632 233
VIII-28	634 <u>235</u>
VIII-29	635 236
VIII-30	636 237
VIII-31	637 238
VIII-32	638 239
VIII-33	639 240
VIII-34	640
VIII-38	643 243
VIII-40	644244
VIII-41	645 245
VIII-46	649 249
VIII-48	651 <u>251</u>
VIII-55	656 256
VIII-57	658 258
VIII-59	660 259
VIII-60	661 260
VIII-61	662
VIII-64	663 261
VIII-66	665 262
VIII-73	672 267
VIII-74	673 <u>268</u>
VIII-76 VIII-80	675 270 679 272

550

Nucleotide sequences

Sequence ID - 93SEQ ID NO: 1

nt: 405 GGATCCTGTGGCCCACAGAGCTGCCCCAGCAGACGCTCCGCCCCACCCGGTGATGG AGCCCGGGGGGACAATCGTGCCTGGGGAGGAGCAGGGTACAGCCCATTCCCCCAG CCCTGGCTGACCTGGCCTAGCAGTTTGGCCCTGCTGGCCTTAGCAGGGAGACAGGG GAGCAAAGAACGCCAAGCCGGAGGCCCGAGGCCAGCCGGCCTCTCGAGAGCCAGAG CAGCAGTTGAATGTAATGCTGGGGACAGGCATGCTGCCGCCAGTAGGGCGGGGACC CGGACAGCCAGGTGACTACCAGTCCTGGGGACACTCACCATAAACACATCCCCA GGCAGGACAGATCGGGGAAGGGGTGTGTACCAGGCTATGATTTCTCTTGCATTAAA ATGTATTATTATT

Sequence ID - 108SEQ ID NO: 2

nt: GGCTTTGACAGAGTGCAAGACGATGACTTGCAAAATGTCGCATCTGGAACGCAACA TAGANACCATCATCAACACCTTCCACCAATACTCTGTGAAGCTGGGGCCACCCAGAC ACCCTGAACCAGGGGGAATTCAAAGAGCTGGTGCGAAAAGATCTGCAAAATTTTCT CAAGAAGGAGAATAAGAATGAAAAGGTCATAGAACACATCATGGAGGACCTGGACA CAAATGCAGACAAGCAGCTGAGCTTCGAGGAGTTCATCATGCTGATGGCGAGGCTA ACCTGGGCCTCCCACGAGAAGATGCACGAGGGTGACGAGGGCCCTGGCCACCACCA TAAGCCAGGCCTCGGGGAGGGCACCCCCTAAGACCACAGTGGCCAAGATCACAGTG GCCACGGCCACGGCCACAGTCATGGTGGCCACGGCCACAGCCACTAATCAGGAGGC CAGGCCACCCTGCCTNTACCCAACCAGGGCCCCGGGGCCTGTTATGTCAAACTGTC TTGGCTGTGGGGCTAGGGGCTGGGGCCAAATAAAGTCTCTTTCTCC

Sequence ID 110SEQ ID NO: 3

ACGAAGACAGCATCTGTGGAATGATTCACATCCTCTCAAGTTAGGAGGATGGAGG CCTGCTTCATTAAGAAGCTGGGGGTAGGGTGGGGGTGGGGAACACTTAACAACA TGGGGACCAGTCAGGGGAATCCCCTTATTTCTGTTTTTGCATATGAGGAACCCTAGA GCAGCCAGGTGAGGCTCTCTAGTTTAATAAAAATCATGGAAAGACTCTTAATGCAG ACTCTTCTTAAGTGTTAATAGGGATTTTTTCAGCTTATTTTGGTTGCAGTTTCCAA TTTTTAAAAATGTTGAGGTAATCTTTCCCACCTTCCCAAACCTAATTCTTGTAGAT GCATTAGTGTTGAACCAATGCTTTCTCATGTCTCAATTCTTTGTATATGCATTCTT TTCAGATGTATTAAACAAACAAAAACCCTTC

Sequence ID - 192SEO ID NO: 4 286 nt: CCGGTAATAGAATAGAAAAGGGAGAGTGTCTTCATGCAATGTGGCATCCTGGATTG

GGTCTCGNNACAAAAACAGGACATTAGTGGGAAAATTGGAAATCTGAAAAAAGTCT
GAATTTTAGTTAATATACCAATTTCAGTCTCTTTGGTTTTTGACAGATGTACCATGGT
GATGTAAGATGTTGACCTTGGGGTAGGCTGGGTGAAGGGTATACAGGAACTCTTTG
TACTATCTCTGCAACTTCTCTGTAAATCTAGTATCATTCCAAAATAAAAGTTTATT
TAATTT

Sequence ID 250SEQ ID NO: 5

GTGGAAGTGACATCGTCTTTAAACCCTGCGTGGCAATCCCTGACGCACCGCCGTGA
TGCCCAGGGAAGACAGGGCGACCTGGAAGTCCAACTACTTCCTTAAGATCATCCAA
CTATTGGATGATTATCCGAAATGTTTCATTGTGGGAGCAGACAATGTGGGCTCCAA
GCAGATGCAGCAGATCCGCATGTCCCTTCGCGGGAAAGCTGTGGTGCTGATGGGCA
AGAACACCATGATGCGCAAGGCCATCCGAGGGCACCTGGAAAACAACCCAGCTCTG
GAGAAACTGCTGCCTCATATCCGGGGGAATGTGGGCTTTTGTGTTCACCAAGGAGGA
CCTCACTGAGATCAGGGACATGTTGCTGGCCAATAAGGTGCCAGCTGCTGCCGTG
CTGGTGCCATTGCCCCATGTGAAGTCACTGTGCCAGCCCAGAACACTGGTCTCGGG
CCCGAGAAGACCTCCTTTTTCCAGGCTTTAGGTATCACCACTAAAATCTCCAGGGG
CACCATTGAAATCCTGAGTGATGTGCCACTGATCAAGACTGG

Sequence ID 299SEQ ID NO: 6

Sequence ID 300SEQ ID NO: 7

Sequence ID 302SEQ ID NO: 8

AGTAGAGACGGGGTTTCACTGTGTTAGCCAGGATGGTCTCGATCTCCTGACCTCGT
GATCCGGCCACCTCGGCCTCCCGAAAGTGCTGGGATTACAGGCGTGAGCCACGGCG
CCCAGCCCCAGCCTGTCACTTAAACTGATAAACGACAGATTAACAGTAGAAAAATT
TTATTTTGCATACATAATGAGGCTTCACAAAAGAGAAGTGAAAACCCAAGTAGGAG
TTTAGGGCTGGGGGCTTATATACCATTTAACAAGGGGTGATAAATTGTAAGAGAAT
AG

Sequence ID 304SEQ ID NO: 9

Sequence ID 306SEQ ID NO: 10

CTTTTCCTCCCGCTGTCCCCCACGGAGGGGACTGCTCTCCCCCGCTGCATCCTTTC
TGTGAGGTACCTTACCCACCTCAGCACCTGAGAGGGTGAAATAGAATTCTAACCTC
GACATTCGGGAAGTGTTTTTGAGAAGTCTCGGTCGGTAAGGGAAGTCTTCCAAGTC
CGTGCAGCACTAACGTATTGGCACCTGCCTCCTCTTCGGCCACCCCCCAGATGAGG
CAGCTGTGACTGTCCAAGGGAAGCCACGACTCTGACCATAGTCTTCTCTCAGCTT
CCACTGCCGTCTCCACAGGAAACCCAGAAGTTCTGTGAACAAGTCCATGCTGCCAT
CAAGGCATTTATTGCAGTGTACTATTTGCTTCCAAAGGATCAGGCCCTGAGAACAA
TGACCTTATTTCCTACAACAGTGTCTGGGTTGCGTGCCAGCAGATGCCTCAGATAC
CAAGAGATAACAAAGCTGCAGCTCTTTTGATGCTGACCAAGAATGTGGATTTTGTG
AAGGATGCNCATGAANAAATGGACNAGCTGTG

nt:

373

Sequence ID - 308SEQ ID NO: 11

AAGTGGGTCTTGCCATCCCTGAACTGNAATCATCCCTAACATATTCATACCTGTTT
TCATTTTAAAAAGTTGGGTCAGTTTTTTTTATTAGTACATGTATTTCTATCCTACTGA
TTTATTTGCTATATCATCTAATTTAGTTTGAATATTCCATAATTTACTTAATTAGT
CCTGTATGGAGACCTAGCTCTTCTCAGTGTCTACTATTATAAACAATGCTACAGTG
AATATTGGTGNATAAATCCATACNCACCACGTACATATCTTAAGTTCTGGAAGAGA
TATTGCTAAACCAGAAGATAACCTGCATTTAAAATTTGACTGCTAGGGNCAGGGNC
ACATTTAATTAAATTAGAACAANGAATGCATAATGNC

Sequence ID 309SEQ ID NO: 12

Sequence ID - 310 SEQ ID NO: 13

nt:564

AATAATGGCCTAATCACTGCATTTTTAAAAAACAAAGTTCAACACAAATGACATTT

Sequence ID 311SEQ ID NO: 14

CCTCTCCTCCATCTAAAGGCAACATTCCTTACCCATTAGTCTCAGAAATTGTCTTA
AGCAACAGCCCCAAATGCTGGCTGCCCCCGGCCAAGCATTGGGGCCGCCATCCTGC
CTGGCACTGGCTGATGGGCACCTCTGTTGGTTCCATCAGCCAGAGCTCTGCCAAAG
GCCCCGCAGTCCCTCTCCCAGGAGGACCCTAGAGGCAATTAAATGATGTCCTGTTC
CATTGG

Sequence ID 314SEQ ID NO: 16

CTTTTCCTCCCGCTGTCCCCCACGGAGGGGACTGCTCTCCCCCGCTGCATCCTTTC
TGTGAGGTACCTTACCCACCTCAGCACCTGAGAGGGTGAAATAGAATTCTAACCTC
GACATTCGGGAAGTGTTTTTGAGAAGTCTCGGTCGGTAAGGGAAGTCTTCCAAGTC
CGTGCAGCACTAACGTATTGGCACCTGCCTCCTCTTCGGCCACCCCCCAGATGAGG
CAGCTGTGACTGTCCAAGGGAAACCCAGAAGTTCTGTGAACAAGTCCATGCTCT
CCACTGCCGTCTCCACAGGAAACCCAGAAGTTCTGTGAACAAGTCCATGCTGCCAT
CAAGGCATTTATTGCAGTGTACTATTTGCTTCCAAAGGATCAGGCCCTGAGAACAA
TGACCTTATTTCCTACAACAGTGTCTGGGTTGCGTGCCAGCAGATGCCTCAGATAC
CAAGAGATAACAAAGCTGCAGCTCTTTTGATGCTGACCAAGAATGTGGATTTTGTG
AAGGATGCACATGAAGAAATGGAGCAGGCTGTGGAAGAATGTGACCCTTACTCTGG
CCTCTTGAATGATACTGAGGAGAACAACTCTGACAACCACAATCATGAGG

Sequence ID 315SEQ ID NO: 17

Sequence ID 316SEQ ID NO: 18

Sequence ID 321SEQ ID NO: 19

Sequence ID 322SEQ ID NO: 20

TAGCATTTGGCCTTTTAAAACATTTGTTTATTTTTTTTTCTGAGAATGGCTAACACA
CTTTATTGAGGTTCGAAATTAATAAAGAAAATAAAAGAAATGTATCTTCATT
CTGTATGTTAGTGTTTTAATTACCCTTAGAATATATGGATAAAAAAATACTATTCTT
TGTCTTGGAGAAGGTAAGAGTCTAGTTAGATGAATAAAGGGTTATCTATGTAGAACA
ACTAGAGAATGAGAAGAGAGCTTATGAGATTGAGTACTACGTTATGCAGTAGAGTA
GCACGTCATCTGCTACTGAGTATGGTGTGATAACATTGTGTAACAGGAAAGTATGA
TCAATATCTACTTAAAATTAAGGACAATATTAGCACTACATTGCTTTATTTTAAAG

AGTTAAGCAGAATAATACATGTTCAAGCATCTGCTAAATCATTAAATATAAGAATA
TAGGGGTTTTCTATAATCTTATTTTCTTTGGAAGAGTACCTCATTTTCAAGANGAG
AAGTTTCTAATTGCCACTTCTTTAAAAATAAAACAGGGTTTTAATGTTCCCAGCAC
AAAAATTAATATCTCTTCAAAAAGTCTCTTGTGATTAAGTTTGAATCCCTTGTCAT
ACTGCTTCTAATATTGACACTGACCTCCTTAGGTATTTTTCAGGGGTTATAATCTT
TTCTTAAGGTATCTTTTTTCAAGAATTGGATACCTTGGGCTT

Sequence ID 323SEQ ID NO: 21

CGCGTCGACTTTTAAAGTCATCTCTATAGGAAGGTGCTGGGCAGGGATCCCAGAGA
AAGAAAGGGTCCAAGACTCCATTAACTGCCCTGGATGAAGGGCACTGCTACAGCAG
CTAGTACCAGAGACTCTCCTATCTCACGGTTGAGGCAGACCCAGGATAGAATAGAG
AATAAAAGGAATGCTTATAGGAAACAATTTTGTATGGAATGCTAGATGGCCAAGCC
TCAGCCTTTGGTCCAGTGCAACCCTTGCCTCGCTTGTCAACAGTGAAAAATTAGTT
TGGTTAGAAGAACCATCTGGAAACACACCAGCTTCTGCTACCTTCATGCTCATTGT
TAAAAAAAGATTAACCAGTGTGAACATTCTGATCTGTTAATTCCAGGGACTGTTTT
CTTTCCAATGGACTGTTTTGTTGGTAGAATAACCCCCAAAAGCTCAAAGCTAAAATG
CATCATCAGTCCTAGTCGGCAGTTCCTTAAGAATGGACTGGCGGCGTGGTTGAGCT
GATATGGAAAAGCTGCACCTTCCTGCAGAAGATCAACTGACCTGCTATCCCACCCC
AAATTCAACCTGAGGTATATTTCAGTGAAGCAGGTAGCTGTTCTTCAAAGCAGA
GAAGCAGTTTTAAGAACCAAAAAGGTAGAGGAAATCTA

Sequence ID 324SEQ ID NO: 22

GTTTGTTACAGGCAGAATTGGATAGATACAGCCCTACAAATGTATATGCCCTCCCC
TGAAAAAATTGGATGAAAATCTGCACAGCAAAGTGAAACACACAGATAATAGGAA
CAAAATGTAGTTCCCATGTGCCAAACAAAATAAATGAAATCTCTGCATGTTTGCAG
CATATCTGCCTTTTGGGAATGTAATCAAGGNATAATCTTTGGCTAGTGTTATGTGC
CTGTATTTTTTTAAAATGGTACACCAGAAAAGGACTGGCAGTCTACTTCTACCATA
GTTAAACTTCACCCTCTTTAATTTCACAACATATTCTTTGGAAGCAGGAAGAATG
CTCATAAAGAGGATCAGACCTTCTTTCCCGTGAAACCAGTATTTGGCGCCATATAT
AAGCCTGGTTAAATTGGTCATCTAAAGCTGTCAAATAAGACATTCTGTGAAAGGTA
AACATCGAAACTGGTTATAAGTAAAACCATCAAGCCAACAACAGGGTCTTGAGATA
ACCTTTGAAGCTTATTGTCTGGCCTGCACCAGAAGATGTCTGCATTACTCATTGCT
AAAAATGTGTACACAGAACTGCACTAGGATTAATTGGTTCAAGAAGAAATTTAAAC
TTACGTTTGGGTTTCCATACAGCACTCTATTGAATACATGCATCTGAATTTAAGTT
GCAA

Sequence ID 327SEQ ID NO: 25

CGGCTACCGACAGAAGGACTATTTCATCGCCACCCAGGGGCCACTGGCACACACGG
TTGAGGACTTCTGGAGGATGATCTGGGAGGGGAAGTCCCACACTATCGTGATGCTG
ACGGAGGTGCAGGAGAGAGAGCAGGATAAATGCTACCAGTATTGGCCAACCGAGGG
CTCAGTTACTCATGGAGAAATAACGATTGAGATAAAGAATGATACCCTTTCAGAAG
CCATCAGTATACGAGACTTTCTGGTCACTCTCAATCAGCCCCAGGCCCGCCAGGAG
GAGCAGGTCCGAGTAGTGCGCCAGTTTCACTTCCACGGCTGGCCTGAGATCGGGAT
TCCCGCCGAGGGCAAAGGCATGATTGACCTCATCGCAGCCGTGCAGAAGCANCAGC
AGCAGACAGGCAACCACCCCATCACCGTGCACTGCAGTGCCGGAGCTGGGCGAACA
GGTACATTCATAGCCCTCAGCAACATTTTGGAGCGAGTAAAAGCCGAGGGACTTTT
ANATGTATTTCAAGCTGTGAAGAGTTTACGACTTCAGAGACCACATATGGTGCAAC
CCTGGAACAGTATGAAATGTGCTACAAAGTGGTACAAGATTTATTGATATATTTCT

GATTATGCTAATTTCAATGAAGATCCTGCCTTAAATATTTTTTAATTTAATGGCAN AT

Sequence ID 328SEQ ID NO: 26

Sequence ID 330SEQ ID NO: 27

Sequence ID 331SEO ID NO: 28

GCCGCGTCGACCTGCATGAGCCACAGTTTCTTGACTGGAGGCCATCAACCCTCTTG
GTTGAGGCCTTGTTCTGAGCCCTGACATGTGCTTGGGCACTGGTGGGCCTT
CTGAGGTGGCCTCCTGCCCTGATCAGGGACCCTCCCCGCTTTCCTGGGCCTCTCAG
TTGAACAAAGCAGCAAAACAAAGGCAGTTTTATATGAAAGATTANAAGCCTGGAAT
AATCAGGCTTTTTAAATGATGTAATTCCCACTGTAATAGCATAGGGATTTTGGAAG
CAGCTGCTGGTGGCTTGGGACATCANTGGGGCCAAGGGTTCTCTGTCCCTGGTTCA
ACTGTGATTTGGCTTTCCCGTGTCTTTCCTGGTGATGCCTTGTTTGGGGTTCTGTG
GGTTTGGGTGGGAAGAGGGCCATCTGCCTGAATGTAACCTGCTCCCGAAGC
CCTGCGGGCCTGGCTTGTTGTGAGCGTTGTTCAACCTGCACCCCTCC

Sequence ID 335SEQ ID NO: 29

CCCGCGTCGACTTTTAAAGTCATCTCTATAGGAAGGTGCTGGGCAGGGATCCCAGA
GAAAGAAAGGGTCCAAGACTCCATTAACTGCCCTGGATGAAGGGCACTGCTACAGC
AGCTAGTACCAGAGACTCTCCTATCTCACGGTTGAGGCAGACCCAGGATAGAATAG
AGAATAAAAGGAATGCTTATAGGAAACAATTTTGTATGGAATGCTAGATGGCCAAG
CCTCAGCCTTTGGTCCAGTGCAACCCTTGCCTCGCTTGTCAACAGTGAAAAATTAG
TTTGGTTAGAAGAACCATCTGGAAACACCAGCTTCTGCTACCTTCATGCTCATT
GTTAAAAAAAAGATTAACCAGTGTGAACATTCTGATCTGTTAATTCCAGGGACTGTT
TTCTTTCCAATGGACTGTTTGTTGGTAGAATAACCCCCAAAAGCTCAAAGCTAAAA
TGCATCATCAGTCCTAGTCGGCAGTTCCTTAAGAATGGACTGGCGGCGTGGGTGAG
CTGATTTGGAAAAACTGCCCTTCTGCAAAAAACACTGGCCTGCTTTCCA

Sequence ID 337SEQ ID NO: 30

Sequence ID 338SEQ ID NO: 31

CTGGACTGCATGACCAGATCTGATGGGTGAGACTCAGGTGGCATGGAAGAGCCGAA
AGAGGATACCATATGTGGGTGCCGGGGGGGATAGGTGAGAAGTACTAGAAGGCGGA
ATGGAAGGACACTTCTGCTCAGCTCTGTGACACGGGCAGGGACCCTGCAGGGCTCA
GGTCCTTTAACACAGCAGCTTCATTCTAACACCAGCAGCGTTGGAACACACGTACA
AGTATGCAGACTAAGCTCTTGCTTGGCTGATACGGCTTTTTTGGGTTTTTAGAGAAC

Sequence ID 339SEQ ID NO: 32

TTTTTTTTAAATAAAGCTGTCGGCACTCAAGGGTAATTTCATATCAGTGTGNTCT
ACAAGCTGGGGGAAAATGAGTTCTAATTGTCANAGCTACCAAATCCTTCACCTTTA
GCATAAAGGTTTAAAGATATCACAAAGATGCCAAGTGATTAATAATGTTTTAAACC
ACCCTTTTTCTGTCTGAAAAAACAACTAAAACAATATTACAACAGTATAGTTACA
GAAGGGTTCTATTTTCATATGTTTTATGCACACTGTGCCTCAAAGGTACTATTTAA
ATATATACTTTTGAGGGGGTGGCTAATGCAGAAACACCCAAGACCTAAGGAAGA
TACAACCCCATTTCTAGGTGTGAGGTCTAAATGCTTCACACACCCACTTGTGACCT
TTTTTCATGAAGAATCATAACACTGTGCAGTGAGAAACAGTGGCAAAGCAATACTG
AAAGCATTTTAAATTATTTACTAGGTTAAAAGGGTGAACTGATACTTTAAATACAT
CAAATTTCATCAT

Sequence ID 360SEQ ID NO: 33

Sequence ID - 361 SEQ ID NO: 34 nt: 622
CTGTNATNGAATCTGCTTGTNACTNAAATGCTAAACTCAATTCTGTAATTCAATAG

Sequence ID 365SEQ ID NO: 37

GTCCCGGAATCGCGGCCGCGTCGACCTTTTCTATGCCTGCTATATAAACAGTACCT TGCAAGATGTCCTGTCTGATATCCACAAAGGGGTATTGTCAACCCCAAGTTCAGAC AGCTTTGTATTCTTCTGTCCCTGGATACATGAATTACTGCCATCTTTACACAGCGC CCTAAAATACCAACGCGAAGTTACCTGCTCAGCTTGAAGCTGCGCTGTACCCTGGA ACCAGCACTTCTGCTGAATGACTCAGGATGAAGCCTCGACTTCTCCTTCCCATCCC ATGCCCAGACCCCAGTGGCTCCTTTCCCAATCTGATCCAGTGACTTTAAGTCCAGC TGTTGCAACCTGGGCATGAGGAGGAGTGCAAGATGGCTTTGTCCTACCTGGAAAGA GGCTTTCTGGA

Sequence ID 366SEQ ID NO: 38

CACCATTTACACACAGTGGGTCCTTGAATAGCATCGTTTTATTCAATGTCATTTTG

Sequence ID - 368SEQ ID NO: 39

329 nt: GAAAGATCTAAAATCGACACCCTAACATCACAATTAAAAGAACTAGAGAAGCAAGA GCAAATTCAAAAGCTAGCAGAAGGCAAGAAATAACTAAGATCAGAGCAGAGCTGAA AGAGATAGAGACACAAAAAACCATTCAAAAAAAAACAATGAATCCAGGAGTTTTTT TTTTAAAAAGATCAACAGAATTGACAGACTGCTAGCAAGACTAATAAAGAAGAGAG AAGCATCAAATAGACTCAATAAAAAATGATAAAGGGGATATCACCACCAATCCCAC AGAAATACAAACTACCATCAGAGAACACTATAAACACCTCTATGCAAAT

Sequence ID 369SEQ ID NO: 40

GAAAGATCTAAAATCGACACCCTAACATCACAATTAAAAGAACTAGAGAAGCAAGA GCAAATTCAAAAGCTAGCAGAAGGCAAGAAATAACTAAGATCAGAGCAGAGCTGAA AGAGATAGAGACACAAAAAACCATTCAAAAAAAAAACAATGAATCCAGGAGTTTTTT TTTTAAAAAGATCAACAGAATTGACAGACTGCTAGCAAGACTAATAAAGAAGAGAG AAGCATCAAATAGACTCAATAAAAAATGATAAAGGGGATATCACCACCAATCCCAC AGAAATACAAACTACCATCAGAGAACACTATAAACACCTCTATGCAAATAAACTAG AAAAT

Sequence ID 370SEQ ID NO: 41

GAAAGATCTAAAATCGACACCCTAACATCACAATTAAAAGAACTAGAGAAGCAAGA GCAAATTCAAAAGCTAGCAGAAGGCAAGAAATAACTAAGATCAGAGCAGAGCTGAA AGAGATAGAGACACAAAAAACCATTCAAAAAAAAACAATGAATCCAGGAGTTTTTT

Sequence ID 371SEQ ID NO: 42

GCCCGGAATCGCGGCCGCGTCGACGTAAGCTCGGCTGAATCCACGGTTCAAGAACA
GGAAAGAAGGCCAAGGCATAGGGAGTGGGGCAGTTGGGTGAATATTAGTACCTTTC
CCTCAGNTNCATTAATTACCCCTGCCTACTCTGCACAAAAGGATNTAACAACAGTT
TCCTTTTTAATGGCCAGGTACAGCTGCTTATATGGANGGGCATTTNTNAATGATAT
CCTTNATCACTGTCTTAATCATCACATNCTTAAAACAATCACTTTATTGTGTTAAG
GAAGATAAAAATGGCTGGGTTCAATTTCCGTTCTGGAAGAAATCGANTNAAAAGGT
AACCATTTAATAATGCANAGGGCANTTTCACTGCAGACCCTAATACTGGAAATTTT
TAAAAACAAATGAAAAACTTCTACTTTTTTCTTCTAAGCTTAACTTTAACCACCCAAAT
TTTCCAGCCACATATCTTCCTAGTCTACAACTGCCTTTAACTTTAAGAGATGCTCA
AAAAAATGTAAATTCTCAAATACATTCTTATTACAATTACTGCTAACCT

Sequence ID 373SEQ ID NO: 43

CCAGTGTGCTGGGATTACAGGCATGAGCCCTGCACCCAGCCTCTTAAACTGATCAT
ATGATATTGGTTCTCAACCAAGGGTGACTTTGCCCCCAGAGGATACTTGGCAATGT
CTGGAGATACTCAGTTGTCATGACTTGGACAGGTGCTACTGTCACCCAGTGGGTAG
AGGTCAGGGATGGTGCTAAACATAGGACAGCTGTCAAGAGAAAAGAATGTACCCAG
CCCCAAATGTCAGTAGGGCTGAGGTTGAGAAACCCAGCTGTAGCTGACGTGTGAAG
GACAGACTGGCCTGGAAGTGTTTTTCTGCCCCTTTCCACCCCTGCATATTAGTTA
AGGCCAAAGGAAAAAAGGAATGCAGGAAATGCCCGTTAAAAATCTTCAAAACAATA
TAAAATGATCAATTCCACTAAAACCCTTTACACATTTAAGTATAAAGGTATTGGTA
GGAAAATTTGTTATTCACTGCTTTTCTCAGTGTCATGAAATAATTATTTCTGCTGT
CAGTTT

Sequence ID 374SEO ID NO: 44

Sequence ID 378SEQ ID NO: 45

CGACTGCGGCTCTTCCTCGGGCAGCGGAAGCGGCGGCGGTCGGAGAAGTGGCCT
AAAACTTCGGCGTTGGGTGAAAGAAAATGGCCCGAACCAAGCAGACTGCTCGTAAG

TCCACCGGTGGAAAGCCCCCCGCAAACAGCTGGCCACGAAAGCCGCCAGGAAAAG
CGCTCCTCTACCGGCGGGGTGAAGAAGCCTCATCGCTACAGGCCCGGGACCGTG
CGCTTCGAGAGATTCGTCGTTATCAGAAGTCGACCGAGCTGCTCATCCGGAAGCTG
CCCTTCCAGAGGTTGGTGAGGGANATCGCCCAGG

Sequence ID 380SEQ ID NO: 46

Sequence ID - 382 SEQ ID NO: 48 nt: 444 GTTAAGGAAGTCAGCACTTACATTAAGAAAATTGGCTACAACCCCGACACAGTAGC ATTTGTGCCAATTCTGGTTGGAATGGTGACAACATGCTGGAGCCAAGTGCTAACA TGCCTTGGTTCAAGGGATGGAAAGTCACCCGTAAGGATGGCAATGCCAGTGGAACC ACGCTGCTTGAGGCTCTGGACTGCATCCTACCACCAACTCGTCCAACTGACAAGCC CTTGCGCCTGCCTCCCAGGATGTCTACAAAATTGGTGGTATTGGTACTGTTCCTG

Sequence ID 384SEQ ID NO: 50

Sequence ID 386SEQ ID NO: 51

CTAAGGGTTTAAAGATGGAAAGAGGCATTGATGAACAGCTGGGGAAGGAGTAGTTT
GAGGTAGATGTGCAGATGGAATGAAGAGAAGGTCTCAAGAAGAGGGTGGAGCCAAA
GAGGGCTGCAGATTTAGAAGGCTAAAGTCTTTAGATGGCTTTGGATAGCCTGTTGT
ATCTTGGACCATGCAGGTTACAGTGGAGCATGGAGTGGGGACAGAAGTGGAGGAAG
GAACCAGGGAACATGGAGTGAGAAGCTAAAGGAAAGTGATGCAGTAGATACATGGC
TCTAAAGTACTCAGGACTTTCAGAGGCTTAAACATAGGGTGACCAACTATCCCACT
ATGCCTGATACTAAGGGCATTCCCTGGATGTGGACCTTCATTCCCCAAATTAGGA
AAGTCTTGGGCATACCAAGACAAGTTGGCCACCCTACTCAAAAGTATGTAAGCTAA

Sequence ID 387SEQ ID NO: 52

Sequence ID 388SEQ ID NO: 53

Sequence ID 389SEQ ID NO: 54

CGACCCGGAATTCGCGGCCGCGTCGACTGAGTTCTTGACAAGAGTGTTTTTCCCTT CCCGTCACAGAGTGGGCCCAACGACCTACGGCACTTTGACCCCGAGTTTACCGAAG

Sequence ID 394SEQ ID NO: 57
GACCGGGATCGCGGCCGTCGACCATTTTAGCCAAGGTGCCTCTATAGGGGTCA

Sequence ID 395SEQ ID NO: 58

Sequence ID 396SEQ ID NO: 59

CTTAAATCTAAATGGACCACATTCTCTACTTAAAAAAATGCTATTAACCATGTGAT
CTTCTCAGTCATGAGGTAATCTGGTGACTACCCTTCCTCAAAGCCAGTTGGGATAT
TCTTTGAATAGAGTAAAACAGTGTTTCTAGGCTGGGAGACACCAGACATAGTTGAG
GACAGAGGTGCTAGAAAATAGGAAGTTTAAAAGCATGTGCGGTGATGCTCAGAGGA
GGTAAACCCCACCCTCATGCTCATAGCTTCCAATCATTTTCTCTAGTTCTTAACTC
TTAAATGTGAGAAATGCTTGAAGATTACTAGTCATCTGAAGAAAGTCTCTTTATTA
AAGATTTTCATAAAAGAGACCAAAGCAGACAAACAGAAAAAAGACATCTTGGGGAAA
AAAACAAGGATAATGGGAAGAAGGAAAGGTTTTAAAAAATTATCAATATCCTCAGG
GGGACAAAATATTATATCCTATAAAGACAGATTTTTATTTTTTTAAAAAAATTAGAAA
GCAAAACAAGCTCCTAAAAA

534

nt:

Sequence ID - 397SEQ ID NO: 60

GACCCGGAATCGCGGCCGCGTCGACGGAAGCTCCTGCCCCTCCTAAAGCTGAAGCC
AAAGCGAAGGCTTTAAAGGCCAAGAAGGCAGTGTTGAAAGGTGTCCACAGCCACAA
AAAGAAGGAGATCCGCACGTCACCCACCTTCCGGCGGCCGAAGACACTGCGACTCC
GGAGACAGCCCAAATATCCTCGGAAGAGGCGCTCCCAGGAGAAACAAGCTTGACCAC
TATGCTATCATCAAGTTTCCGCTGACCACTGAGTCTGCCATGAAGAAGATAGAAGA
CAACAACACACTTGTGTTCATTGTGGATGTTAAAGCCAACAAGCACCAGATTAAAC
AGGCTGTGAAGAAGACGCTGTATGACATTGATGTGGCCAAGGTCAACACCCTGATTCGG
CCTGATGGAGAGAAGAAGCACATTTTAAACTGAGTCCAGCTGCCTAATTCTGAATA
TATATATATATATATATATCTTTTCACCATAA

Sequence ID 399SEQ ID NO: 62

Sequence ID 400SEQ ID NO: 63

GAAGAAGCGCGAAGAGCCGTTAGTCATGCCGGTGTGGTGGCGGCGGCGGAGACTGC
GGGCCCGTAGCTGGGCTCTGCGAGGTGCAAGAAAGCCTTTGAGGTGAAGGTGTATG
AAAGTCATCATAACAGATGTTTTCCAAAAACTTGTAGAAGGTTGTGAAAAAACTAC
TAGGATCACGCGGCATGTATTGAGCATATAGGTTGCTGTAGATGAATGTTCTTAGC
TGTCATGTTTAAAAAATACTTCTGCTTCGTTACCTCAAGTGTGGCATGCAGCATTTT
GGAAGGAAAATTGAAGACGTGTTCAAGAAAACATGAACAGAAGCAAATGATGAAAA
TGAGCATTTTACTTGATGTTGATAACATCACAATAAATTATGGAGAAAAATACATA
TTTTGGCTAACTTTTAATTGCTGAACAATAAAGTGTTTTCTTTTAAATCNAAAAA

Sequence ID 401SEQ ID NO: 64

Sequence ID 402SEQ ID NO: 65

GACCCTATTCTCAGGATGAAAATAATACACTAGTAATAGTCTGCTCTGTTGGTTAA
CTCCTCGTAAGGAGGTACAATTAAAATGCTGTAGTGTTGCAAGGGAAGGAGGAA
GAATCATATTCCTTCACTAGCAGGATCAAGAAAGCTTTTATAGAAATATACAAAAT
CTTCACTTCTTGAAGGATTGGTAAAATTTAATAGCCAACATTGGGCACTTATTCAT
TCTCTGAGTAAATATTTATTGCATGCTTATCTTGTATCAACATTGNGATGAAAGCN
CAAGAATGAAAGAGGAGGGAGAATGTTTANAGAATAAGGCTGAAACACAGATTTTG
TAGGGAGCGTAGGGGGAGACTGANAAAACAG

Sequence ID 403SEQ ID NO: 66

AAGACACCTGATAGATTGTCTTGTATTATTTTTCCTTTGCCTTCTTACAATCTCAG
TGATTAGAATTGGGCTGAAAACAATACATCAAATTCTCAGCAAAATCCTTATGGGT
TGCTGGATACCGAGGGTTTTTAAGATCTTTAGACTTCACTATATAGAACAAATGTT
GAATGGGAATTTTCTTTATTTCTATANCGTTTNG

Sequence ID 405SEQ ID NO: 67

CCCGGAATCGCGCCGCGTCGACGATGAGCATTTTTTCATGTGTCTTTTGGCTGCA
TAAATGTCTTCTTTTGAGAAGTGTCGGTTCATATCCTTTTGCCCACTTTTTGATGGG
GTTGTTTTTTTCTTGTAAATTTGTTTGAGTTCATTGTAGATTCTGGATATTAGCCC
TTTGTCAGATGAGTAGGTTGCGAAAATTTTCTCCCATTTTGTAGGTTGCCTGTTCA
CTCTGATGGTAGTTTCATTTGCTGTGCAGAAGCTCTTTAGTTTAATTAGATCCCAT
TTGTCAATTTTGGCTTTTGTTGCCATTGCTTTTGGTGTTTTAAAAGTCCTT
GCCCATGCCTATGTCCTGAATGGTAATGCCTAGGTTTTCTTCTAGGGTTTTGATGG
TTTTAGGTCTAACGTTTCAGTCTTTAATCCATCTTTTAAAAGTCTCTTCACAGTAC
ATGAGTAGTAGTGACACCAATAATGTCAGAGCAGGGAACTCCCAGGTTCTGCCCAT
CCACAAAAACAACAAATAAGCTGGCAAAAACTTTAAGAATCAACTTTTGCAGATCT
CTGAAATCTAGTCAAAACTTAAACAGAGGAAAAGATTAATAAAGACNGGCTGCCTGA
GATAACACTAACACACAC

Sequence ID 406SEQ ID NO: 68

CATCAAATAAATAAATAAATTTTAAAAGTCACAGCATTGAATTTTTAAATGT
TTGGGATGATAAAGCACCTGCTTATCATGAAGCTANAGAAATTCAATGACACGTTT
GCCAGGGTCTTTGCTAGTGATGTTGGAACAAGTCTGTAATGCTGATGAAACATCAC
TGTTCGGGCATTATTGCCCCAGAAAGACACTGACTGCAGCTGATGAAACAGCCCTT
CCAAGAATTAAGGATGCCAAAGACCAAATAACTGTGCTGAGATATACTTACGCAGC
AGGCATGCATAAGTGTAAACTTGCTGTTATAAGCAAAAGCTTGCGTTCTCACTGTT
TTCAAGGAGTGAATTTCATACCAATCCATTATTATGCTAATAAAAAGGCATGGATC
ACCAGGGACATCTTTTCAGATTGGTTTCACAAACATTTTTGTACCAGCAGCTTGTGC
TTACTGCAGGGAAGCTGACTGGATGATGACTGCAAGATTTTTTATATCTTAACAA
CTGTTGTGCTCATCCTCCAGCTGAAATTCTCATCAAAAATAATGTTTATGGCTCAC
ACCTGTAATCTCAACACTTTGGGAGGATTGCCTGACCCAGGAGTTCAAGCCCACCC
TGGGCAACACAGCAAGACCCAACCTNTC

Sequence ID 407SEQ ID NO: 69

TTTTAAAAATCATAAAACGTTTCTTACAAAAGAGCATTACATTNTGCACACTGCTC
TGAACAGATGCCAGGGACATGTGGACTATTGTTACTTTTCCTCCCTGTCCCACCCC

Sequence ID 408SEQ ID NO: 70

CCATCTCCAAATTTAGTATTCATTCTGTTTAGCATATTATCAGTTGCCATCTATTT
GTTTTAACTGATTACTTGAATCTGATTAAACATCACAGAAATGGGCTTTGATAAGA
ACAATATTGAATAAGAAATTTTAAATAACAAAACAGCTTATAGAAAAATTCAGCAT
AACTTTTCCATCACCTTCACCACCCTTGCCTTTTATTATCCTGTCCTGTATCACTG
CTTTCTGTTAGCAGTGTTGTGTGAGGTTAGGATTTGGGCAGGAAAGCAAAAGCAACC
ACCCGTCATTTTCCCAGAATGAAGGGTTTGACGTAGGATGTAGACTTTGTATAGTA
GTTGGGAGAGCTGTGGGAGTGAAGGTCAGGGATGTCACCTACAGAAGTCAGGGAAT
CTGCCACCAGAGATCCTGCATCAGAAACAGCCAACAGCGTGCTTCTGAAGAACTAG
TGGGGAAGTGGCTATAATTCTTAGGAATCCCAGCAAGTCCGCACCACTGTCTCAGT
CTACAGCAGTGGAGAAAGGGGTTTCCAGGAGCTCTCTGGAAAGTTCCTGCCCACAC
TTTGCAACAATCTTCAGAGGATAATGGGCTTCTCTTCCAGCTTCCACACCAACAA
GAGTGCCTTTCATCGGCCAACTCTAACCTGGAACCCTATGGCAGAGGGGATTTAGG
AGACAGTTTGTNATGTCTGTGGAATGCAAATGAANANGTANCAATGCTTANTTGAC
AGCGGNCATACACAAATNTNGAAA

Sequence ID 409SEQ ID NO: 71 GATCCGTNGACT

Sequence ID 410SEQ ID NO: 72

CTCTTCCCAGCCCCTGAGCCCAGCCCCTTCCCAAGTGGTGCCAGACAAAAAACTAC
ATGGCCCTTTCGTGTCTTGGGGGTGGAAAGGGAGGGATGAATTGGGGTGATAGAAC
CCTGGTGAATTCAGAGTAATCTTTCTTTAGAAAAACTGGTGTTTTCTAAAGAAACAG
GATAGGAGTTTAGAGAAGGCACCAAAGCTTTCACTTTGGTTTGGCACCAGTTTCTA
ACCATCTGTTTTTTCTACCCTAGCTATCTTTTATTGGTAAAATATAAATGTATAAT

AATTTTTGATTCTCCATTTTCCAAAAGTAAGAGACTCCAGCATGGCCTTCTGTTTG CCCCGCAGTAAAGTAACTTCCATATAAAATGGTATTTGAAAGTGAGAGTTCATGAC AACAGACCGTTTTCCATTTCATCTGTATTTTATCTCCGTGACTCCACTTGTGGGTT

Sequence ID - 411SEQ ID NO: 73

505 nt: TGGAGCTGAAAAATTCCTATTACCTAGGGGCATCACAACGCATTGCATTTCGCCCG TGTTTGGGATGATGCTGGTGTAAACCTACTATGCTGCCAGTCATGTAAAAGTATAG CACACACAATTAGTAGGTAATGCTTGCAAATAATAATGAAAGACTCTGCTACTGGT TTATGTATTTACTATGCTATACTTTTTGTCATTACTTTAGAGTGTACTCCTACTTT TTTTTTTTTTTTTTGAGATGGAGTTTCACTCTTGTCCTGTAGGCTGGAGCGAAN TGGCGCGATCTCGGCTTACTGCAACCTCCACCTCCTGGGTTCAAGCGATTCTCCTG TTTGTATTTTTGGTAGAGACAGGGTTTCACCATGTTGGCCAGGCTGGTCACCAACT CCTGACCTCAGGTGACCCGCCTCCTCACCTCCAGAGTGTTGGGATTACAGGNGTGA G

Sequence—ID-412SEQ ID NO: 74

ATAAAAATTAGCTGGGGGTGATGGGCCCTGTACCCCAGCTACTCGGGAGGTGAGGT AGGAGAATCACTTGAACCCGGGAGATGGAGGTTGCAGTGAGCCAAGATCGTGCCAC TAATAATAAAAAAGGAATAACATAGCTAGGAATAAATTTAATCAAAGAGGTGAA AGACTTATACACTTAAAACTACAAAAAAAAAATCACTGAAGGAATTATAGACCCAA ATAAAAATAAATAAAAGACATTCTGTGTTTTAGGGAAAGAAGACTTAATATTGTT AAGATGTCAATACTACCCAAAGTGATCTACAGATTCAACATAATCCCTATCAAAAT TCCAACAGCCTACTTTGTAGAAATGGAAAAGCCAATTTTCAAATTCAGATGGAATT TCAAAGAACTCACACTTCTCTATTTATAATTTACTACAAAGTTATAGNATCAAAGT CGACGCGCCGCGATCCGGGC

Sequence ID 413SEQ ID NO: 75

CACAGTACTCCATTTTGGGGTCCAAACTGTAATGCTCAAAATAATAAATGCTTACA CGAAAATTATTTATTGAGAATATTCATATAAAAATTACCTAAAGCAAAGTAAAAAA AGTAAAATCAAGGTGGTATATTTGAAGTGAATGGTGATTGGAAATTTTTAGCTGTA

TACCTTATTCCCACACACTCTTGGGCTGACCTTTATTTTATCAATAAGCTCAATAT TACTTTGTTTAAAATAAGATGCTTCAGCAAAAGTCATTCTCTCTTTAACCATATAA TTTAAAAACTCCTCTTCACGATTGATAGCAAAATCAGAAACGTTAGGGCACCAGTG AGTTGAAAAACTGGTCTTAAGTTGGAAAAACTATTATTAATAATATTATCCTATC AAGAAGAAAAGATAATACCCATTTGTTCTAT

Sequence ID 414SEEQ ID NO: 76

CTCAGACTCTTTCTGCCCTAATGGCCATTACTATCCAGTCTGTATTGCTACAAGGG ACCCACTGGTACCCCTTTTAGATTCTATCAAAAGGAACAGGGTTTTCCTAGAGGCA GGCAGCCTGGTGGTATGGCACAGCAGAAGCTTACTGCTAATGAAATGGGAACCTCC CCCTCCCTTGTGGTTTCAGCACAGAACCTGAATGCCAGGAAAAATTCCTGGGCCAA TAGGGTCACTTTTGATTGAGGCAAAGGGGTCCTACTGTAAGTGGAAAAGACTCACT CCCCTAACATAAGTTTTCACTGTGGTGGGATGGTGCCGCCCGATATGCTTGATATG CTTTTCCTTCCACATGTTAAGCTAGGAAACCTAACAGGATGTCAGCAGGGCAGTTA ACTCTGGACTCANAGCCCTCAAGGGCATGTGGCANAACCTCATGGCATNCAAGACC Α

Sequence ID - 415SEQ ID NO: 77

596 nt: GTATAATTGATTCTTTTGAACCTAAAGTATAAGACTTCACGATTAGAAAAAATTA TCCAAAGACTAATGTAATTAAGTGAGGAAAAGGTGCTGGAGGAACTGGATAACCAC ATGGAAATGTATGAACCATGACCTCTATGTCACATACTATATAAAAACTTAATTT GAGGTGTATCACAGAGCTAACTGTGGGGGCTAAAACGTTGAAGCCTTTGGATGGCC GCACAAGAGATGTCTGCATTCATAACCTTGGGGAGGGTATGAACATTTCTTGGTAA CATGCAAAAAGCACTAACTGTAAAAGAGAACAGTTGGTCAGTTGAATTTCATGAAA CATTGTAAACTTCTGCTAAACAACTGACACCATTAAGAATGTGGAAAAAGGCTGGG $\mathtt{CTTGAGGCCAGGAGTTTGAAACCAGCCTGGGCAACATGGCAAGACCCCGACTCTAC}$ AAAAATATTTTTAAAAATTAGTTGGGTGTGGTGATGCACTCCTGTAGTCCTAGCTG CCAGGANGCTAAGGNGGAAGGATCACTTAACCCTGG

Sequence ID 416SEQ ID NO: 78

CTGGTGGCGGCGGTCGTGCGGACGCAAACATGCAGATCTTTGTGAAGACCCTCACT GGCAAAACCATCACCCTTGAGGTCGAGCCCAGTGACACCATTGAGAATGTCAAAGC CAAAATTCAAGACAAGGAGGGTATCCCACCTGACCAGCAGCGTCTGATATTTGCCG

GCAAACAGCTGGAGGATGGCCGCACTCTCTCAGACTACAACATCCAGAAAGAGTCC
ACCCTGCACCTGGTGTTGCGCCTGCGAGGTGGCATTATTGAGCCTTCTCTCCGCCA
GCTTGCCCAGAAATACAACTGCGACAAGATGATCTGCCGCAAGTGCTATGCTCGCC
TTCACCCTCGTGCTGTCAACTGCCGCAAGAAGAAGTGTGGTCACACCAACAACCTG
CGTCCCAAGAAGAAGAAGGTCAAATAAAGGTTGTTCTTTCCTTGAAGGGCAGCCTCCTGC
CCAGGCCCCGTGGCCCTGGAGCCTCAATAAAGTGTCCCTTTCATTGACTGGAGCAG

Sequence ID 417SEQ ID NO: 79

Sequence ID 418SEQ ID NO: 80

Sequence ID 419SEQ ID NO: 81

Sequence ID 420SEQ ID NO: 82

CTTCATTTGAAATGGTTGAATCTGCTGTGTAATAAAGTGGTTCAACCATGATTAGG

387

nt:

Sequence ID 421SEEQ ID NO: 83

Sequence ID 422SEQ ID NO: 84

Sequence ID - 423SEQ ID NO: 85

TGTTTCTCNAGGGCGAGAGGCTGTCTTANAGCACCATTCTCTGGCCCTNGTCCCAT
GAGAAGGAACCGCACTCAGGAGCCACACTCTCCCACTNCCCTTGCCCANAAGACTC
ACAGAGGCACGGAGCTGGCTGTGGTGAGAGGAGGTCCANCAAATTCCTGTCTGCA

nt:

420

Sequence ID - 424SEQ ID NO: 86

CGCAGAATGGCTCCCGCAAAGAAGGGTGGCGAGAAGAAAAAGGGCCGTTCTGCCAT
CAACGAAGTGGTAACCCGAGAATACACCATCAACATTCACAAGCGCATCCATGGAG
TGGGCTTCAAGAAGCGTGCACCTCGGGCACTCAAAGAGATTCGGAAATTTGCCATG
AAGGAGATGGGAACTCCAGATGTGCGCATTGACACCAGGCTCAACAAAGCTGTCTG
GGCCAAAGGAATAAGGAATGTGCCATACCGAATCCGTGTGCGGCTGTCCAGAAAAC
GTAATGAGGATGAAGATTCACCAAATAAGCTATATACTTTGGTTACCTTGTTACCT
GTTACCACTTTCAAAAAATCTACAGACAGTCAATGTGGATGAGAACTAATCGCTGAT
CGTCAGATCAAATAAAGTTATAAAATTG

Sequence ID 425SEQ ID NO: 87

Sequence ID 426SEQ ID NO: 88

Sequence ID 427SEQ ID NO: 89

TTCCAATCTTCGTGTTCACTTTAAGAACACTCGTGAAACTGCTCAGGCCATCAAGG
GTATGCATATACGAAAAGCCACGAAGTATCTGAAAGATGTCACTTTACAGAAACAG
TGTGTACCATTCCGACGTTACAATGGTGGAGTTGGCAGGTGTGCGCAGGCCAAGCA
ATGGGGCTGGACACAAGGTCGGTGGCCCAAAAAGAGTGCTGAATTTTTGCTGCACA
TGCTTAAAAACGCAGAGAGTAATGCTGAACTTAAGGGTTTAGATGTAGATTCTCTG
GTCATTGAGCATATCCAAGTGAACAAAGCACCTAAGATGCGCCGCCGGACCTACAG
AGCTCATGGTCGGATTAACCCATACATGAGCTCTCCCTGCCACATTGAGATGATCC
TTACGGAAAAGGAACAGATTGTTCCTAAACCAGAAGAGGAGGTTGCCCAGAAGAAA
AAGATATCCCAGAAGAAACTGAAGAAACAAAAACTTATGGCACGGGAGTAAATTCA
GCATTAAAATAAATGTAATTAAAAGG

Sequence ID 428SEQ ID NO: 90

TGCAGGATCCGTCGACTCTAGATAACATGGCTAGAAAAGAGAATGAAAAAGTTGGA
ATTTTTAATTGCCATGGTATGGGGGGGTAATCAGGTTTTCTCTTATACTGCCAACAA
AGAAATTAGAACAGATGACCTTTGCTTGGATGTTTCCAAACTTAATGGCCCAGTTA
CAATGCTCAAATGCCACCACCTAAAAGGCAACCAACTCTGGGAGTATGACCCAGTG
AAATTAACCCTGCAGCATGTGAACAGTAATCAGTGCCTGGATAAAGCCACAGAAGA
GGATAGCCAGGTGCCCAGCATTAGAGACTGCAATGGAAGTCGGTCCCAGCAGTGGC
TTCTTCGAAACGTCACCCTGCCAGAAATATTCTGAGACCAAATTT

Sequence ID 430SEQ ID NO: 92

Sequence—ID-431SEQ ID NO: 93

CGCTGGGTGCCTGCAGCGCCTCCCTTGTCTCATATGGTGTGTCCAGCACTCTATTG
TTGTAAACTGTTGNTTTGNCTGACCTAAATTNTCTTTACTAAACANATTTAATAGT
TNAAAAAAAAAAAAAAAANANCA

Sequence ID 432SEQ ID NO: 94

Sequence ID 433SEQ ID NO: 95

Sequence ID 434SEQ ID NO: 96

Sequence ID 435SEQ ID NO: 97

577

552

nt:

nt:

Sequence ID 436SEQ ID NO: 98

Sequence ID - 438SEQ ID NO: 99

GTCGACAGGGATGACATAACTATTAGTGGCAGGTTAGTTGTTGGTCACTTTCAACT
CTGGGTTCAAGCGATTCTCCTACCTCAGCCTCCCGAGTAGCTGGGATTACAGGCAT
GCACCGCCACACCTAATTTTCTATTCTTAGTAGAGACGGGGTTTCTCCCTGTTGGT
CAGGCTGGTCTCGAACTCCCGACCTCAGGTGATCTGCCTCAGTCTCCCAAAG
TCCTGGAACCACAGACATGAGCCACCACGCCTGGCCCCTTTTAAAATATTTCTGCT
CATTGATGATGCACCCCAGTCACCCAAGTGCTCTGATGGAGATGTATAAGGAGATGA
ATGCTGTTTTCATGGCTGCTAATACAACATTCATTCTGCAACCCCCAAATCAAGAA
GTAATTTTGACTTTCAAGTCTTATTATTTAAGAAATATATTTTGCAAGACTATAGC
TGCCATAGACCGTGATTCCTCTGATGGATCAGACAAACTAAAATGAAAACCTCCTG
CAACGTATTCATCATCTTAGATCCCTGAGGAATCGCCACACTGACTTNCACAATGG
GTGAACTGGGTTACAGT

Sequence ID - 441SEQ ID NO: 100

TGCATCTGCTGAAGCGAGAACCCCATTCTGCCACCCACCAGGATGCCCATTCTCC
AGGACTTCTCCAACTTACTATTAGACTAAACCAGAACAAGCAAAACTGTATTTA
TGCAAGCAAAATTGATGAGAAAATTATATTCAAATAAAGCAAAAATTA

Sequence ID 446SEQ ID NO: 102

CGGACTCCTGTGCTAATTGTCAGCTTACATATCATTGTATAGAGACTGTTTATTCT
GTACCAAACTGATTTCAAAAGTACTACATNGAAAATAAACCGGTGACTGTTTTTCT
TCATAAAGTTCTGCGTTTGGCATCTTCACTCTTTCCAAAATGTATCTGTACATCAN
AAATGTCACTATTCCAAGTGTCTTTTTAGTGTGGCTTTAGTATGGCTTCCTTTTAA
TATTGNACATACATTGNATCTTTGTTTTATGGNAATAAGTAATAAAAATGTAGACT
TCATATTTTGTACAAAATGTCCTATGTACAGAATAAAAAAGTTCATAGAAACAGCC
NANAA

Sequence ID 447SEQ ID NO: 103

Sequence ID - 448 SEQ ID NO: 104 nt: 329
TACGCACACGAGAACATGCCTCTCGCAAAGGATCTCCTTCATCCTCTCCAGAAGA
GGAGAAGAGGAACACAAGAAGAACGCCTGGTGCAGAGCCCCAATTCCTACTTCA
TGGATGTGAAATGCCCAGGATGCTATAAAATCACCACGGTCTTTAGCCATGCACAA
ACGGTAGTTTTGTGTGTTGGCTGCTCCACTGTCCTCTGCCAGCCTACAGGAGGAAA
AGCAAGGCTTACAGAAGGATGTTCCTTCAGGAGGAAGCACCACACACTCTG
AGTCAAGATGAGTGGGAAACCATCTCAATAAACACATTTTGGGTTAAAA

Sequence ID 450SEQ ID NO: 105

Sequence ID 452SEQ ID NO: 106

TTTGGCTTTGCCTCTAGGCATTAGATGTTATCTTTGGAGGCATCCTTCTATGAGCA
TTCATTTTTGGACCAAGCCTGGATTTACAATTCTATTACTGGCCCAGACTTCATTT
CTATCCAATTTCATTCCACTGTGCTATAGTTTACAACATATAATTTGACTTATAAA
TAATTCCTGACTATGGGTTTAAAGACTGAAAATGGATCAATAGAAACTTTGAAAAT
GTTAACATCTTGATTGCTTTTCTCAGTGTAGAAATGGACAATGTTTAGCTTAAAAA
CTGCATGTTTTTAATGAGATACGGGGTTGAAAGACTTATTCCTGGAATTTATTGTT
CTGGAGAAAGCCTGTTGCTATCTGCCATACCTTGGTTTACTTTTGTGCAAAATGAGC
TTCTTTTTAAGTAATGAGCTCTTTCCATGTTCAGCTTAAATTGCTGTCTTAGACAC
TTCATCAGGGTTCCCTGCTCTGCCTCATTCCCCCTTTTTGCTCACTTGCAGCCTTTG
ACATAATCCTGGGAGGCAATTGGCATCATACATATTTTTGCTTTGTAATCTCCTGCT
TTGATTCTGACTGGGACCCAGC

nt:

747

Sequence ID - 453SEQ ID NO: 107

GGATCTAAGACCAGCCTGGCAGCCACCAGATGGTGATTCTAGTCCTGGCTCAGTCA GTAATAGGTCACTGACCCCAGAGAAATCAATTCAGCCTCCCCAGGTCCTTGGATTT CTTTCTGTGAAAATGAAAGCATAGGTAGGAATTTCCCATGGAACAGCTAGCAGAGG AGAAATATTAAAAGTCAGGAGACTCATGCTATAGTTTTCATACTTCATTACAACAA TGTTGTTTAGGACAAGTGAGTTAACCTGTTAGCTTCCTCTATATAAAATGGAAAGT CATTAAAAACCTACATAGCAGGGTTCTTGTGAAGATCAAGTGATAATGTAGGAAGC ATGTACAAATGTCACATTCTGCCGTCACGTAATGGTCCTCACAGCTTGAGGTAGCA TTTAGCATGTGTCATGATTTAGTACAAGGGTTGGCAAACTGTTGCTCTTGGATTAA GTCTGGCTCATTGCCTGTTTTTCAAAGAAAAAATTGTATATGTGTGTATATATGT TATATATAGGTACACACACATATGTGCTATATATAGCATATATACACACATAATAT ATAAACATGTACATATATGCATTATATATATACCGTGTATAATATCTCCAGTCCT CATGACCAGCCATGCTTGTTCATTTACATTTGCATACTCTATGATTGCTTTCATGC AACAATGGCAGAGTTGAGTGATTGTTTTGCACAGANACTGTATGGCCCACTAAACC TAAAATATTAATCTCTGCC

Sequence ID 454SEQ ID NO: 108

CTCCTGCCGGGCTCGTGGCGGCTTCTGTCCGCTCCGCGGAGGGAAGCGCCTTCCCC ACAGGACATCAATGCAAGCTTGAATAAGAAAAACAAATTCTTCCTCCTAAGCCATG GCATATCAGTTATACAGAAATACTACTTTGGGAAACAGTCTTCAGGAGAGCCTAGA TGAGCTCATACAGTCTCAACAGATCACCCCCCAACTTGCCCTTCAAGTTCTACTTC AGTTTGATAAGGCTATAAATGCAGCACTGGCTCAGAGGGTCAGGAACAGAGTCAAT TTCAGGGGCTCTCTAAATACGTACAGATTCTGCGATAATGTGTGGACTTTTGTACT GAATGATGTTGAATTCAGAGAGGTGACAGAACTTATTAAAGTGGATAAAGTGAAAA ATATGACTTTTTTACACCATCTTCTGTTATTCATTGCTTTTGAAGAGAAGCATAGA AGAGACTTTTTATTTATT

Sequence ID - 458SEQ ID NO: 109

682 nt: ATTGTAAGAACAAGCCGTACCCAAAGTCTCGCTTCTGCCGAGGTGTCCCTGATGCC AAGATTCGCATTTTTGACCTGGGGCGGAAAAAGGCAAAAGTGGATGAGTTTCCGCT TTGTGGCCACATGGTGTCAGATGAATATGAGCAGCTGTCCTCTGAAGCCCTGGAGG CTGCCCGAATTTGTGCCAATAAGTACATGGTAAAAAGTTGTGGCAAAGATGGCTTC CATATCCGGGTGCGGCTCCACCCTTCCACGTCATCCGCATCAACAAGATGTTGTC CTGTGCTGGGGCTGACAGGCTCCAAACAGGCATGCGAGGTGCCTTTGGAAAGCCCC

nt:

536

AGGGCACTGTGGCCAGGGTTCACATTGGCCAAGTTATCATGTCCATCCGCACCAAG
CTGCAGAACAAGGAGCATGTGATTGAGGCCCTGCGCAGGGCCAAGTTCAAGTTTCT
GGCCGCAGAAGATCCACATCTCAAAGAAGTGGGGCTTCACCAAGTTCAATGCTGAT
GAATTTGAAGACATGGTGGCTGAAAAGCGGCTCATCCCANATGGCTGTGGGGTCAA
GTACATCCCCAATCGTGGCCCTCTGGACAAGTGGCGGCCCTGCACTCATGAAGGCT
TTCAATGTGC

Sequence ID 459SEQ ID NO: 110

TCCCGGAATCGCGGCCGCGTCGACCTTGTCCTTGAGCGTCAACCTTCTTTCCCTGA
AGTGGCTGGGGTTCCTGTTTCCTTCTTTGATTGACAACTTGTGTTAACCCTCGCAC
ATCTCTGGGCCAATTTTTGCTTGTAAGTCTTTCCGGAGACCCCTGGAATTTAAATC
ATTAGCACCGCGCCCTTCCCCGAAGAGTCTTCGAAGGGTTGCCGCTTTTCGGTGGC
GCAGTTCTCGCGAGAAGGTGACTTTCTTTCTCGGTATTTCCTGGTTTCCAGAATCC
TTAGCGCGAGGCGGAAAAAAATATTTCTCCCAGCTTGTTGTTGATGCCGCGATTTTGA
CTGAGACTTCTTCCCACGATTTCTGTTTTTTGCTTCTCCAAGGAAAATGGCAGCTCC
CGAGCAGCCGCTTGCGATATCAAGGGGATGCACGAGCTCCTCCTCGCTTTCCCCGC
CTCGGGGCGACCGAACCCTTCTGGTCAGGCACCTGCCGGCTGAGCTTACTGCTGAG
GAGAAAGAGGACTTGCTGAAGTACTTCGGGGCTCAGTCTGTGCGGGTCCTGTCAGA
TAAAGGCATTGACAAACTNCATCAACTGAAACTTTTAGTCATACTTTTAATCG

Sequence ID - 460SEQ ID NO: 111

Sequence ID 461SEQ ID NO: 112

TAGGAGGCTTATTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCT ACGCCAAAATCCATTTCACTATCATCATCGGCGTAAATCTAACTTTCTTCCCA

Sequence ID 462SEQ ID NO: 113

TCTTTATCAAGTTGAGAAAGTTCCTCCCCTCTATTCCTAGTTTGCTAAGAGTCCTT
CTATCCTATTTCTTAATGGTTTAGTAGATGACTCTGTGGTACTTTGAAGGTTGTTT
GCAGAATTTCCATGCCATAGGCAATTTACCTTTCCTTGACATTTGAAGGATTGATG
TTGGTGCCAAGTATAGAATCTTCACAGAGTCCTCCTGTAGCTTCTAAAGGTTTAGC
TTGAAAATGTTAATTGCTTAACGCTAGTAAGTGAGAGAAAAAGCTGGGGATAAATT
TTGTATCTTGCTTATATTTCAGTTCCCACCTCTGTCCNGACNAAACCCCCATATAT
AA

Sequence ID 463SEQ ID NO: 114

TAGTTTACATATCCCAACCTTTAAAAATATTCCTCTTATTAGCTTTATATTCACTT
TATAGAAGTTGAGTTTTAATTAAAATTCTTGGCATCCTGAAGTATGTCACATAGCA
TGTGCTCCTTATAAATATGTTGATATCTCAGAAGACAGCATCCCGGTTTTCATTTT
ATAAAGTACCATACTTAAGAATGCTGTAATACTTATCTTTTATAACATGTTTCCTT
CGCTTTGCTTGNCTTTTATGNCATCAGTTTTAACTGTTTACTTCATTTAACAGNTT
ACATCATNCAACAGTTTACTTCATTAAACAGTAGGTGGAAAAATAGATGCCAGTCT
ATGAAAATCTTCCCATCTATATCAAAAATACTTTCAAGGATATACTTT

Sequence ID - 464SEQ ID NO: 115

nt:

615

CCTTCTGGAGACTTCTAATGAAACANATTTCCTGATTGGCATTAATGAANAGTCA Sequence ID 469

Sequence ID 471SEQ ID NO: 117

TCCCGGGAATCTGCAGGATCCGTCGACT

Sequence ID 472SEQ ID NO: 118

GACAGTGCCCAGGGCTCTGATATGTCTNTCACANCTTGNAAAGTGTGAGACAGCTG
CCTTGTGTGGGACTGAAAGGCAAGATTTGTTCCTGCCCTTCCCTTTGTGACTTGAA
GAACCCTGACTTTGTTTCTGCAAAGGCACCTGCATGTGTCTGTGTTCTTGTAGGCA
TAATGTGAGGAGGTGGGGANACCACCCCACCCCCATGTCCACCATGACCCTCTTNC
CACNCTNACCTGTGCTCCCTCCCCAATCATNTTT

Sequence ID - 473 SEQ ID NO: 119

nt:

694

Sequence ID 474SEQ ID NO: 120

Sequence ID 475SEQ ID NO: 121

Sequence ID - 476SEQ ID NO: 122

nt:

476

CAGAATCTTTTCATAGGCTGAATGTTGCTCCACAATGTGTCCTTTGACTATCTCTG
GCTAATTATTTTTAATCTCTTCTCAGCTTTTCCAAGAACATAACGTTAACCAAA
GATCTTAGGCCATTCACAACTCTTTTGTAAAAATTAATGTGGATGTGAAACGAGGC
AACAAATCCTGAAGTAGAAAGTTATTCCTGGCCAGGCACGGTGGCTCACGCCTGTA
ATCCTGGCACTTTGGGAGGCCGAGGTGGGTGGATCATGAGGACAGGAGATCGAGAC
CATCCTGGCCAACATGATGAAACCCCATCTCTACTAAAATACAAAAAATTAGCTGG
GCATGGTGACGCGTGCCTGTAGTCCCAGTTACTCGGGAGGCTGAGGCAGGGAATT
GCTTGAACCTCGGAGGTGGGAGGTTGCAGTGTCCCAGTTCCCACTCC
AGCCTGGCAACAGAGCAAGACTCCATCT

Sequence ID 477SEQ ID NO: 123

AAACAGAAAGTTTCTTCTAAAGGCATGATTCAGTTAAGTCATTCTTAAGTGTTAAA
AAATTGTGAAAAATGTGCCTGTAATCCCAACACTTTGGGAGGCCGAGGCAGA
TCACGAGGTCAGGAGATCAAGACCATCCTGGCTAACAAGGTGAAACCCCGTCTCTA
CGAAAAATACCAAAAACATTAGCCGGGCGTGGTTGTGGGCGCCTGTAGTCCCAGCT
ACTTGAGAGGCTGAGGCAGGAGAATG

Sequence ID 478SEQ ID NO: 124

TTCTTGGGATATTGATGACTACTGTCTGAGAGGTGCTGTGGGGAGATTTTCAGGAT
TGTGTGGTCTTTGAGGGGGGGTGTTTTTTTAAGACAACATTGACCACTGTCCACTGT
CCACATGATCATTGTAAAATTGCAATGCCGCATGCTAGTTGGTTACATAAGACATA
ATTCCAGTGATTGAAGGTGGTTACACTGTATGGTGGTGTTCAAGATGGCACTGG

Sequence ID 479SEQ ID NO: 125

Sequence ID-481SEQ ID NO: 126

Sequence ID 482 SEQ ID NO: 127

Sequence ID 483SEQ ID NO: 128

CGNTAACGTGCAATCCGCCGCACGCCAGCAAACTGGACAAACTCCGGGATCTCATC
GAAGCGATTGAGCACCAGTACCAGAGTAATACCGGACTGATGTAACGAGGCGAGTC
GCTCATCCAGCTTGCTGACGTGAGGCAACATCCAGGCCATCGAACGGNTCATCAAG
AATCAACAAGTCAGGCTCCGACATCAGCGCCTGACACAGCAGGGTTTTTCGCGTCT
CGCCAGTGGAAAGGTATTTAAAGCGTCNGTCGAGGAGGGCGGTAATACCGAACTGC

TGCGCCAGTTGCATGCAACGCGGTGCATCCTTTACTTCATCCTGAATGATCTCAGC
CGTAGTGCGTCCGGTGCCATCTTCGCCAGGGCCGAGCATATCGGTGTTATTCCGCT
GCCATTCGTCGCTGACGAGTTTTTTGCAATTGCTCGAAGGAGAGACGAGTGATGTGG
GAAAACTGGCTTTGCCGTTCACCTTTCAAAAGCGGGAAGTTCCCCCGCCAGCGCGC
GGGCCAGGGCCCGAT

Sequence ID 484SEQ ID NO: 129

TTTTTTTTTTTTTTTATTCTATTAAAAAATGTTNNTGAAAAAAGATACTTAAATTTTAA
AGATAACTNAATTCCTAANGATTTAAAATAATCCAAGCAGAGATGAAAGANCAAAT
GCAAATGCNTAAAAAGACCCCANAGCATTGTTAGCAAAAAGCAAATATAGTTAGCC
AAGCATATATATNTCATAAAAGCAATAANAAGGCNTAAAGCAAGTTTGGGGAGAGC
TTATTTAAAACTTGTAAAAATCATTTGAATTTTTAAAAGTTTTCAAAC

Sequence ID - 485 SEQ ID NO: 130

nt:

551

TTTGGAACACAAAGTTCCCTTTTTAGAAGAATAGGTATTGAGCCCTTGAGCGTGGG
TAGAAAGATAGAGACAGAGTGATTTGCAAAATAATGGAGGATCATATTTATATATG
AATTTTCACTTATTTGAACTTTCAGATATCANCTTNAAAANCTTTGGTTTAAGTAA
AGTNTNTTAATGAGACTCCTTGGATGAAAGTAACCAAAACCAGTAAAAATAAGGTA
ATAAGGATGTAATAGTTTCTTATGGACACTCAACAGCTAGAATGCAGTTAGTCTCA
GAAAAGAATTAGAACAAATAACTGGAAGGCCATCAGGAGTCCAAAACCATCACTCT
TTTATATTTTATATTTTTTTTCTCTCTTCANATGAGCATTCTCTTTCTATGTCC
ATATGGTANAAGGCGGCAGCTCCATAGATTATGGCTTCAGATGTTACAGTTCCGCT
NAATGCAGGGACAGACTTGCTATCTTTCAGTCCCCTTTACATATCCTGGGGAGAGAG
CAAATGATTGACTGGCTTGAGTCAGGTGCCCGTTCCCATTCT

Sequence ID - 487SEQ ID NO: 131 nt:224

Sequence ID - 488SEQ ID NO: 132

nt:

349

AGTGACAAGCCATTGAGTCTTAAGCCTTACGGCTTCCTATAAAATCACTAATTTCG
TGTGTGTTTGTGTAGGTTACGTTATATATAGGATTCGTGTTCGCCGTGGTGGCC
GAAAACGCCCAGTTCCTAAGGGTGCAACTTACGGCAAGCCTGTCCATCATGGTGTT
AACCAGCTAAAGTTTGCTCGAAGCCTTCAGTCCGTTGCAGAGGANCGAGCTGGACN
CCCTGGGGGGGCTC

Sequence ID 489SEQ ID NO: 133

TTAACAGCTGCATAGAGTTTTAAAAGTACATTATATTTTGTCAGACAAGTAAAATA
TCTGTTTTTCACGCAAAAAAAGCCATGAAATACGTAATTTTTTAAAGACAAAAAAT
CATCTTTTGAGTTTGCTCTTTGGTTTTTCTTCATTCCTTTTGAGGATTGGGAAAAC
AGAAAGATTCTTTGATTTGGGTAATGAAGAGGTAATTTTGGGACAGTGTGGTGGTAC
CAGGAAGAAAGAGGATTGGAAAGGCCAGTACTGTTTTAGTTGCTCGGCACTGTTGG
TTTTGTTTTAATGTGGTTGCCCTGTCCACTACATGGTTCTATCAGTAGTGTAATCC
ATTTTCAATGTAAAGCTCTTTTAGTTTTTTGTCATAGACATAAATTAATATTTTGAG
AGGCATCCCTCACCTGTTCATTTCTTCTGTGTTGAAATGAAGTACTTAAAATTACC
GTTATACATGAACTTTGTGGACTGTAAGATTTGTTATATATGTTCAAATGCCTTTT
AGCTGGCTTTTTAATTAATATGCCTGTTTTTGAGTGCTTAATACAATGTAATGNGGA
TTGTAAATCATACCTATTTTAAATCATTCCTTCCTGTATATTTGNACTCAGAGAGC
CTTATTTTATTCTTCCAGC

Sequence ID - 491SEQ ID NO: 134

nt:

382

Sequence ID 492SEQ ID NO: 135

Sequence ID 493SEQ ID NO: 136

Sequence ID 494SEQ ID NO: 137

Sequence ID 495SEQ ID NO: 138
TTTC

Sequence ID 496SEQ ID NO: 139

CTCGCTGGCGGAGGCCACGGGCTTTCCACAGCGCGGGGGAACGGGAGGCTGCAGG

Sequence ID 497SEQ ID NO: 140

GAAGACCTCACATCTGAGAGCTCATCTGCGTTGGCATTCTGGAGAACGCCCTTTTG
TTTGTAACTGGATGTACTGTGGTAAAAGATTTACTCGAAGTGATGAATTACAGAGG
CACAGAAGAACACATACAGGTGAGAAGAAATTTGTTTGTCCAGAATGTTCAAAACG
CTTTATGANAAGTGACCACCTTGCCAAACATATTAAAACACACCAGAATAAAAAAG
GTATTCACTCTANCAGTACAGTGCTGGCATCTGTGGAAGCTGCGCGAGATGATACT
TTGATTACTGCAGGAGGAACAACGCTTATCCTTGCAAATATTCAACAAGGTTCTGT
TTCAGGGATAGGAACTGTTAATACTTCCGCCACCAGCAATCAAGATATCCTTACCA
ACACTGAAATACCTTTACAGCTTGTCACAGTTTCTGGAAATGAGACAATGGGAGTA
AATATTACACAAAATACTTATTCATTGNGGTTATTTTTATACAGTAGTGAGAAGAAT
ATTGTTCCTAAGTTCTTAGATATCTTTTTTTTGGATGTGCAAAAAATTTTTGGATTGA
CAGTAACTTGGGTATACATGACACTGAAATGCCTTACTTTGGATGA

Sequence ID 499SEQ ID NO: 141

Sequence ID - 500 SEQ ID NO: 142

nt:

Sequence ID 502SEQ ID NO: 143

Sequence ID - 503SEQ ID NO: 144

nt:

109

Sequence ID - 504SEO ID NO: 145

nt:

374

Sequence ID 505SEQ ID NO: 146

Sequence ID 506SEQ ID NO: 147

Sequence ID - 507SEQ ID NO: 148

nt:

521

Sequence ID 508SEQ ID NO: 149

AAGCTCATGATTTTAAATGTATTTTTCTAATAAACTATACTCCCATTTAAAAAATCA CCAATACCTTAATGTTTCAATTATATAAGCTAATTAAAAATAAAGGCTGGGCGTGG TGGCTCACTTTGGAAGACCGAGGCAGGCAGATCACCTGAGGTCAGGAGTTCGAGAC CAGCCTGCCCAACATGGAGAAACCCCATCTCTACTAAAAATACAAAATTAGCCAGG CATGGTGGCACATGCCCGTAATCCCAGCTACTGGGGAAGCTGAGGCAGGAGAATCA

Sequence ID - 509SEQ ID NO: 150

nt:

575

Sequence ID 510SEQ ID NO: 151

Sequence ID 512SEQ ID NO: 152

GTGAGCGGTGGTGTTTATTCTTCCGTGGAGTTAAGGGCTCCGTGGACATCTCAGG
TCTTCAGGGTCTTCCATCTGGAACTATATAAAGTTCAGAAAACATGTCTCGAAGAT
ATGACTCCAGGACCACTATATTTTCTCCAGAAGGTCGCTTATACCAAGTTGAATAT
GCCATGGAAGCTATTGGACATGCAGGCACCTGTTTGGGAATTTTAGCAAATGATGG
TGTTTTGCTTGCAGCAGAGAGACNCAACATCCACAAGCTTCTTGATGAAGTCTTTT

Sequence ID 513SEQ ID NO: 153

TTTTTTTTTATAAACTCCAATCATTTCCAGAGCTACTTAGCTCAGCATCTTTTTT
TTCCACGCTCTTAAGTTGTGTTTATACATTTTTGATACAGTTAGATTGTTTTTGTC
ACATTCTTCATTCTATCCTGGGATCCCCCAACCACCTAAGTGGATTTTTTGATAAT
TTGCATGCTTTAAGGATAACTCTTCATTCTGNAAAGGGCTATGGGTTTTGGCAAAT
GCAGAGTCATGTATCCAAGATTACAATATCGCACAGAAGAGTTTCATCACTATATA
AAACTCACCAGTCTTCCTCCTATTCAACCATCTCCATGCCTTCTTCCCAGCCCTAA
CTCCTTAAAACCACTCATATCTTTACTATTGCTATAGTATTGCCTCTTTCCACCATG
TCATATAAATGGAAACATACAGTATTAGTCTTCTCAAACTAGTTTCTTTTACCTAA
CAACATGCATTTAAGATTCATAGTGTCTTTTAATGACTTGATAGATTATTTCTTT
TAGCTGAATAATATTGCATCTTATAGATGTAACCGTTTGTATATCCATATTTTCTC
ACAGCCTATGACTTGNCTTTTGATTCTCTGAACAGGCCATTCACAAAGCAGAAGTT
TTAATTTTTATAAAGCTAATGNATCAACTT

Sequence ID 515SEQ ID NO: 154

CCTGGATGACAGCATATCTGTTTATAGCTCAGTTTACTGAATACTTTAAGCCCACT GTTGAAACCTGCT

Sequence ID - 518SEQ ID NO: 155

nt:

502

Sequence ID 519SEQ ID NO: 156

CTGCGATNGAGTTTTGAGAGGAAGGANTAAAGTNCTCATCTCNGACGGTGAGAAAG
ATCATNACTAAGGAAACGCAGGGTTGGAAGCAGTGCTGANTGTCCAGTTGAGTTTC
ATGANCAAACATTTGCTGTGGGACCAGTTTTCATGGNGGTTTGTCATTTTTTTCCAG
CTGCCTGGAGCTGCTTGGTTGAAGGCACAGAATAATCAGGATTAATTGTTNAACTT
GTATGAATTTCTTTATTTTAAAATAGGAATAATATCTGCCTTGGGAGCAAGTTGTA
AGAGTTAACTGAAAGCTTNAGGAAAAACTTTCCCTTGCTATTTAAGTAGGGCTTTA
CAAGTTACAATTCTATCACAGTTTTAAGATTATAAAC

Sequence ID 521SEQ ID NO: 157

GCGGCGCANCTGCGGATCCANAAGGNCATAAACGANCNGAACCTGCCCAANNCGTG
TGATATCACCTTCTNAGATCCAGACNACCTCCTCAACTTCAAGCTGGTCATCTGTC
CTGATGAGGGCTTCNACAAGAGTGGGAAGTTTGTCTCAAAAAA

Sequence ID - 523SEQ ID NO: 158

nt:

585

Sequence ID 524SEQ ID NO: 159

CTTTTGCCAGTAGGCCCCCTGAGTAGGTTCCTCTATCTTTTGGCATGACCCCAGAA
GTCTTTGATAACTTCCTTGCTTTCTGATGTGACAAGACATCCAGGGCCAGATTGTC
CATATCCTGCCCCGGATGCACGATGCACTGTTTCTCCAAGAATCCCTGTGTCCTTT
GCTGATGATGCCATGATTTTAAGTTCTCTAATATAGTTTTATCTCTTTTGTTTCAGA

Sequence ID 525SEQ ID NO: 160

Sequence ID - 526SEQ ID NO: 161

nt:

516

Sequence ID 527SEQ ID NO: 162

Sequence 529SEQ ID NO: 163; 660nt

Sequence ID 529SEQ ID NO: 164

Sequence ID - 530SEQ ID NO: 165

nt:

660

Sequence ID 532SEQ ID NO: 166

Sequence ID 533SEQ ID NO: 167

Sequence ID 534SEQ ID NO: 168

GAAAATCTATATGTTTCAAAACCACTTGCCATCCTGTTAGATTGCCAGTTCCTGGG ACCAGGCCTCANACTGTGAAAGTA

Sequence ID 560SEQ ID NO: 169

Sequence ID 561SEQ ID NO: 170

CTCAGGGTGATCTCTGAACCCAAACTTGCCCCAAAGAAGGTTGCTCTGTCCTCCC
ACATCCCCATCTCCCCTAGGGCCTTGTTGGGGAAGAGGCTCCTCCATCTTTCCCA
AGTCACACCATCGTTTCCTACGTGGTCTGGACAAGAGCAAGAGCACCACCTTGTCCC
CACCTTCTCCAGAGCAGCCAGAACCCACCTCAGGTGCCTTCCCCATCCGGTGCAGT
TAAGGCACTTCTGCCAGCACCATGGTATGAGCACTAGACTTGGAGTTAAGATTTGA
GAGCCCCCTCTGTCACTGTGGAAGCTTGAGCATGTTGCTTGATCTCTCTGAACCTT
GTGTTTCTCATCTGTGAAAGGTGATAATGTGGGGCTGCTGTGAGATTTAAAGGACA
TAATGCACCTACGGTCCAAGCACTGCCTGGAATACAGCANAAGCTCAACAGATACT
GGACAACCCATCCCCTTAGTAGAGGCACTAACCATGTGACCCAAGGCAAAAGTGCT
TAAAAAAA

Sequence ID - 562SEQ ID NO: 171

nt:

580

ATTGCATGCAAGTTTGCTGAGCTGAAGGAAAAGATTGATCGCCGTTCTGGTAAAAA GCTGGAAGATGGCCCTAAATTCTTGAAGTCTGGTGATGCTGCCATTGTTGATATGG TTCCTGGCAAGCCCATGTGTTGTTGAGAGCTTCTCAGACTATCCACCTTTGGGTCGC TTTGCTGTTCGTGATATGAGACAGACAGTTGCGGTGGTGTCATCAAAGCACTGGA CAAGAAGGCTGCTGGAGCTGGCAAGGTCACCAAGTCTGCCCAGAAAGCTCAGAAGG

CTAAATGAATATTATCCCTAATACCTGCCACCCCACTCTTAATCAGTGGTGGAAGA
ACGGTCTCAGAACTGTTTGTTTCAATTGGCCATTTAAGTTTAGTAGTAAAAGACTG
GTTAATGATAACAATGCATCGTAAAACCTTCAGAAGGAAAGGAGAATGTTTTGTGG
ACCACTTTGGTTTTCTTTTTTTGCGTGGCAGTTTTAAGTTATTAGTTTTTAAAAT
CAGTACTTTTAATGGAAACAACTTGACCAAAAATTTGTCACAGAATTTTGAGACC
CATTAAAAAAAGTTAAATGAG

Sequence ID 563SEQ ID NO: 172

Sequence ID - 564SEQ ID NO: 173

nt:

671

Sequence ID 565SEQ ID NO: 174

CTTGGTTCCGCGTTCCCTGCACAAAATGCCCGGCGAAGCCACAGAAACCGTCCCTG

Sequence ID 566SEQ ID NO: 175

Sequence ID 567SEQ ID NO: 176

CTCATGGCGGCCAATGTAGGCCCAAAACTTCCTCAAGTCAAACTCTCCAGGCCCAC
CTTCTGCTTCCCGGTGGCATCAACAGGCCCAGCTTTGACTTGAGAACAGCCTCTGC
AGGCCCTGCTCTTGCCTCCCAGGGGCTTTTTCCAGGCCCAGCTCTTGCCTCATGGC
AGCTGCCCCAGGCCAAATTTCTGCCTGCCTGCCAGCAGCCTCAACAGGCACAGCTC
CTCCCTCACAGTGGCCCATTTAGGCCCAACTCATGACTGTGAGGCCATTTCCAGGC
CTAGTGCCTGCCTCGTGGCTGACTCTTGAAGCCCAAAACTTCCTCAAATCAGCCTT
TTGCCCAACTTCTGTCTACTGTCGGACTCTACAGGTCAGCCTCTGCCTCACAGTGG
ACCCTCCAGACCCAGATGGTGTCTNCTGTGGCATCCTCAGGCGAAGCTCCTGCCTT
TCGGCAGCCTCTCCAGGCCCAGCTCCTCCTGCTCCAGGCTTCTCCCAGGCTCTGA
ACTTTCTCAGGTCTCCCTCTTTTTCCCAAGGCTGAGTTAGTAG

Sequence ID 568SEQ ID NO: 177

Sequence ID 570SEQ ID NO: 178

Sequence ID - 571 SEQ ID NO: 179

nt:

457

Sequence ID 574SEQ ID NO: 181

Sequence ID - 575SEO ID NO: 182

nt:

209

CAGGATATCGAGACCATCCCAGACAGCATGGTGAAACTCCGTCTCTACTGGAATAC
AAAAAGTTAGCCGTGTGTGGGGCACGCGCCTCTAATCCCAGCTATTCGGGAGGCT
TAGGCAGGAGAATTACTTGAACCCGGGAGGCGAAGGTTGCAGTGAGCTGAGATCGC
ACCATTGCACTCCACCCTGG-CGACAGAGCAAGACTCCGTCT

Sequence ID - 576SEQ ID NO: 183

nt:

541

CAGCCAACCCAGAAGGAGCCAGTCTACAACTATGCCTGATCCTCCTCATGGCAGGCCACGAAGCATTGCTGCCATGTGTTGAATTATAAAACCCACATTGCTTTTTGAACCC

TGTTGCGGGTAAAAATAACCAAATTATCAGTCCTTGGAAACCCAGGCAATCAAGTG
AGTACAAGGTAAAGATAAGTATGGTTTAGAGGAGAAATTATGTTCCTGAACTGGTG
TCCTTTGATGGCAGCGTCAGCCTTGCTAAGTCAGAGTAGAGGGAGCAGTGACCTTA
ATAAGCTTTGGTGAGCATCATGTGCACGCGTGGGTGGGAGTCCCTTTCACTGATGC
TTTTAAAAGTGCTTTTGCAGACCCTGGAAGGGATCCTCCACACATATGAGGTGTGG
GACAGGTAGGCCAGAGAGGATTAGCCCTGCTTTCGAGACTAGAAATCTACAGTCCT
GAAGGAGCAGTAATTAATTGGTACACCTGTCAGGGCCAGCCCCCAGGTCTCCTGGC

Sequence ID 577SEQ ID NO: 184

Sequence ID 578SEQ ID NO: 185

Sequence ID - 579SEQ ID NO: 186

nt:

502

CGAATAGCCAAGTGGTCTGACAAGATCGAGAGTAATGAGGCCCATACTTTAGTACA
GTCTTGAATGGCCAGATGGTGCTGGGCATACCCCAACCAGAGATATGTAAGTCTTT
ATGTTGTCAAAATTTCCCAGAAACATGAATTTCCCACTAAGATTCATTAAGGAAAA
CTAGAATGAAAACAAAAACGTTCCTTGTATAATATTCATTANAAAGAAATGAAGAA
GGCCGGGCATGGTGGCTCACGCCTGTAATCCCAGCACTTTGAGAGGCCAAGGTAGG
CAGATCATGAGGTCAGGAGTTTGAGACCAGCCTGGCCAACATAGTGAAATCCCGTC
TCTACCAAAAATACAAAAAAATTAGCCGGGCATGGTGGCACACCCTGTCATCCCA
GCTACTCAGGAGGCTGAGGCAGGAGAATTGCTTGAACCTGGGAGGTGGAGGTTGCA
GTGAGCTGAGATTGCACCACTGTACTACAGCCTAGGTGACAGTGCAAGACTCTG

Sequence ID - 580 SEQ ID NO: 187

nt:

316

Sequence ID 581SEQ ID NO: 188

CTTCATGAGTGCCCGGTTGCCCAAGTCAAAAACCTGGGAGTGATATAAACTCCCCA
CACATCCAGTCAGTCACTCATCAACTCTATTGATTCTG-CTGCTAAATATATCTCA
ATTGTATTAACTTAAACATATGCATAATACATCTTCTTCTTCACTGCATTTTTGTG
GGCTGCACTTACCTTTCAGGTAACAACAACACTGGCCCCTCTTGCCCTTCTAGTCA
GAAGTGCCAAAATGATGAGAGGCTAGCCATGACAAACCCACAGCCAACATTACACTG
AATGTGCAAAACTGGAAGGGCATCCAAACAGAGGAGG

Sequence ID 582SEQ ID NO: 189

GCCCTACCCCAGTCCTCAGAAAAGTTCCTCTCCCTGGATCCTCTTTTTCCTTCATG
AGTGCCCGGTTGCCCAAGTCAAAAACCTGGGAGTGATATAAACTCCCCACACATCC
AGTCAGTCACTCATCAACTCTATTGATTCTGTCTGCTAAATATATCTCAATTGTAT
TAACTTAAACATATGCATAATACATCTTCTTCTTCACTGCATTTTTTGTGGGCTGCA
CTTACCTTTCAGGTAACAACAACACTGGCCCCTCTTGCCCTTCTAGTCAGAAGTGC
CAAAATGATGAGAGGCTAGCCATGACAAACCCACAGCCAACATTACACTGAATGTGC
AAAACTGGAAGGGCATCCAAACAGAGGA

Sequence ID - 583SEQ ID NO: 190

nt:

631

Sequence ID 585SEQ ID NO: 191

Sequence ID 586SEQ ID NO: 192

GTAAACTGTTCTCTCCGAGGGAAAAAATGGAAGTTATCCTCACAGTTCACTGCCGT
GGTATTTCTTCTGTCCCATGCTTTGCATGACTGCCATGGTACAGCCTTGTTTCAAA
CTGTTCACTGTGATCTGTGGGTCTTTGAGTTTCAGTGAGTTTGCTGAAATGTCGAA
GAAGTAGTTCCAAACTTCAATGTTCAATGAAATTTTTTGTTCAAGTTTGAAATGGAG
AGAGCAGCTTTAAAAAGGTACTAAGCCTTTTACAAATTGGTGAGTACTGGCACATGA
GAT

Sequence ID 587SEQ ID NO: 193

Sequence ID 588SEQ ID NO: 194

Sequence ID 589SEQ ID NO: 195

Sequence ID 590SEQ ID NO: 196

Sequence ID 591SEQ ID NO: 197

Sequence ID 592SEQ ID NO: 198

TACTCAATGAAAAACCATGATAATTCTTTGTATATAAAATAAACATTTGAAAAAAA AAAAAAA

Sequence ID - 593SEQ ID NO: 199

nt:

565

CAGGATCAAGGTGAAAAGGAGAACCCCATGCGGGAACTTCGCATCCGCAAACTCTG
TCTCAACATCTGTTTGGGGAGAGTGGAGACAGACTGACGCGAGCAGCCAAGGTGT
TGGAGCAGCTCACAGGGCAGACCCCTGTGTTTTCCAAAGCTAGATACACTGTCAGA
TCCTTTGGCATCCGGAGAAATGAAAAGATTGCTGTCCACTGCACAGTTCGAGGGGC
CAAGGCAGAAGAAATCTTGGAGAAGGGTCTAAAGGTGCGGGAGTATGAGTTAAGAA
AAAACAACTTCTCAGATACTGGAAACTTTGGTTTTGGGATCCAGGAACACATCGAT

CTGGGTATCAAATATGACCCAAGCATTGGTATCTACGGCCTGGACTTCTATGTGGT
GCTGGGTAGGCCAGGTTTCAGCATCGCAGACAAGAAGCGCAGGACAGGCTGCATTG
GGGCCAAACACAGAATCAGCAAAGAGGAGGCCATGCGCTGGTTCCAGCAGAAGTAT
GATGGGATCATCCTTCCTGGCAAATAAATTCCCGTTTCTATCCAAAAGAGCAATAA
AAAGT

Sequence ID 594SEQ ID NO: 200

Sequence ID - 595SEQ ID NO: 201

nt:

98

Sequence ID 596SEO ID NO: 202

Sequence ID 597SEQ ID NO: 203

362

Sequence ID 599SEQ ID NO: 205

GACAAAAGAACCATTTGGATACATAGGTATGGTCTGAGCTATGATATCAATTGGCT
TCCTAGGGTTTATCGTGTGAGCACACCATATATTTACAGTAGGAATAGACGTAGAC
ACACGAGCATATTTCACCTCCGCTACCATAATCATCGCTATCCCCACCGGCGTCAA
AGTATTTAGCTGACTCGCCACACTCCACGGAAGCAATATGAAATGATCTGCTGCAG
TGCTCTGAGCCCTAGGATTCATCTTTCTTTTCACCGTAGGTGGCCTGACTGGCATT
GTATTAGCAAACTCATCACTAGACATCGTACTACACGACACGTACTACGTTGTAGC
TCACTTCCACTATGTCCTATCAATAGGAGCTGTATTTGCCATCATAGGAGGCTTCA
TTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCTACGCCAAAATC
CATTTCACTATCATATTCATCGGCGTAAATCTAACTTTCTTCCCCACAACACTTTCT
CGGCCTGTCCGGAATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCACAT
GAAACATCCTATCATCTGGAG

Sequence ID - 600SEQ ID NO: 206

nt:

595

TTCAAATTCTTGNTAANAGTCTTTGTTCTGAATTTTACTTTGTCTGTTATTCCTAT
AGCCTTTCCAATTTTCTTTCGCTTGGATTTTACGTGATAAGTTTTTTCCCCATTT
TACTTTTANCAACTCTATATTTTTTAGTTGAGGTTGGGTTTCTTGTAAACAGCATA
TAATTTGGGTTTTTTAATCCAATCTGAAAATTAATGTCCTTAATTTTTGTGTTTATA
CCATTTACACATAATGTACTCATATATAAGGTTTAACTGAAACCTACTATCTTGCT
AGTTGTGCTCTACTTGAATTTTTTTTTAGTATTCTGTTTTAATTGACCAACATTTG
ACTGTATCTCTTTGTGTAATTCTTTTACAGGTTGCTGTAGGCATGACAATATATAC
ACTTAACTTTTCTCAGTACACTGAGAGTTGAAATTGTAGTACTTCGAGGAAAACAT
AGAAAACTTGCAATGATATCGGTTACATTTTACCACCTCCATATGTTGCAATTATT
AAATGTATTAGATCTGCCTACCTCGAAAACCCATCAGTCTTTTAACTTTGCTCTCA
ATGGTGATTCATATTTTTAAAAAAAACTTGAGGCAA

Sequence ID - 601 SEQ ID NO: 207

nt:

522

Sequence ID 602SEQ ID NO: 208

Sequence ID - 603SEQ ID NO: 209

nt:

624

GACACACGAGCATATTTCACCTCCGCTACCATAATCATCGCTATCCCCACCGGCGT
CAAAGTATTTAGCTGACTCGCCACACTCCACGGAAGCAATATGAAATGATCTGCTG
CAGTGCTCTGAGCCCTAGGATTCATCTTTCTTTTCACCGTAGGTGGCCTGACTGGC
ATTGTATTAGCAAACTCATCACTAGACATCGTACTACACGACACGTACTACGTTGT
AGCCCACTTCCACTATGTCCTATCAATAGGAGCTGTATTTGCCATCATAGGAGGCT
TCATTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCTACGCCAAA
ATCCATTTCACTATCATATTCATCGGCGTAAATCTAACTTTCTTCCCACAACACTT
TCTCGGCCTATCCGGAATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCA

Sequence ID - 605SEQ ID NO: 210

nt:

338

ACCTGAGGCCTCGGTGGGGCCAGTGCGACGCTGGCTTAAGGAGCTGGAGGGGTTCC
TAATACACATTTAATTCAGTTTCTCTTCCCTAAGAGGCTGCCGGAGTTGGGGCCTC
CTCCAGCAGAGACCCTCGGACCCCTGCAGGGCCTGGACTTGGGGTGAACAGGGCTT
CAGTCAGCGCAAGTATTCCATTTGCATTTGGTAATTTTTCATGCCACCTATTTATG
AATATAAAATCTTTATACCAAATCTATTTTTTAAAACATGGAAAAGTTGCCTTTA
TGGAAACTTGGCAGAGCCAGAGTGTACACATTCCTAAACCATTAAACAGATTTCTA
TA

Sequence ID - 606SEQ ID NO: 211

nt:

556

Sequence ID 607SEQ ID NO: 212

Sequence ID 609SEQ ID NO: 213

Sequence ID 610SEQ ID NO: 214

GCTCTGACCCCAGTTGGAAATGTATCTGTACTTTGTCCGGCTTCCACTCAAGGACC
ATTTATGACATTGCTTGGTGTCAGCTGACAGGGGCTCTGGCCACAGCTTGTGGGGA
TGACGCGATCCGCGTGTTTCAGGAGGATCCCAACTCGGATCCACAGCAGCCCACCT
TCTCCCTGACAGCCCACTTGCATCAGGCCCATTCCCAGGATGTCAACTGTGTGGCC
TGGAACCCCAAGGAGCCAGGGCTACTGGCCTCCTGCAGTGATGATGGGGAGGTGGC
CTTCTGGAAGTATCAGCGGCCTGAAGGCCTCTGAGCTACCTCGACTTTGGACAGAG
TAATGACTCCCCAGAAAACGTCATATAAGACTTTACCAGCCCCTGAGAGGACCAGG
AGGAGCATCCTTGACCTTCATTTAACTTGGCTCACTTCTCTTCANACTTGGGTAGA
AGTGCAGAGCCACAAAATTGCTTTCCTTCCCCGCCTTTGACATGAGGCCTTCAGTA
AAG

Sequence ID 611SEQ ID NO: 215 TGCAGGATCCGTCGACT

Sequence ID - 612SEQ ID NO: 216

nt:

576

TCATATCCAGCCAAACTAAGCTTCATAATTGAAGGAGAAATAAGATATTTTCCAGA CAAGCAAATGCTGATGAAATCCATCACCACCAGACCTGCCTTATAAGAGCTCCTGA GGGAAGCACTAAATATTGAAAGGGAAGAACTTTATGAACCATTTCAAAAACACATT TAAGTNCACAAAGCAG

Sequence ID - 613SEQ ID NO: 217

nt:

341

CCTTATTTTACAGGTGAAAAACCACGAATCAGATAGATTTTTATTTGCCCAAGTCA
CATAATATTAAGAACAGGCCAAGTGTGGTGGCTCATGTCTGTAATCTGAGCACTTT
GGGAGGCTAAGGCGGGTGGATTTCCTGAGCCTAGGAGTTTGAGATCAGCCTGGGCA
ACATGGCGAAACCTCATCTCTACAAAACATACAAAAATTAGTCAGTGTGGTGGTGA
GAGCCTGTAGTCCTGGCTACTCGTGAGGCTGAGGTGGGAGCATCACCTGAGCCTGG
GAAGTCGAGGCTGCAGTGGCAACAGAATGGGTAACCTGGACATCAGAGTGAGACCC
TGTCT

Sequence ID 614SEQ ID NO: 218

Sequence ID - 615SEQ ID NO: 219

nt:

379

TAAATTTAAAACATTTTAATTAGCTGGCATGATGGCATGCACCTGTAGTCCTACCT
ACTTGGGAGGCCAAGGCAGGAAGATTGCTTGAGCCCAGGAGTTTGAGCTTACTGTG
AGCTGTGATCACACCACTGCACTCCAGCCTGGGTGACAAAGGAAGACCGTATTTCT
AAAAAATAAAAAATACAAATACAACTACAAACTAGCACTAGACCAACAGTGACTAT
GTACCATGAACTGAGGAATATTATTAATTCCACCATTTGCATCTGAGGTTAACAAT
ATGTCAATGACTTAAATAACATCATATCTCTGAGAGTAATTTCCCATTTCCA
TGACAAATGTTAGATAATTTTCCATTTTTTCCATTCAACAAAA

Sequence ID 617SEQ ID NO: 220

Sequence ID - 618 SEQ ID NO: 221

nt:

598

Sequence ID 619SEQ ID NO: 222

Sequence ID 621SEQ ID NO: 223

Sequence ID 622SEQ ID NO: 224

Sequence ID 624SEQ ID NO: 225

TGCAGGATCCGTCGACT

Sequence ID 625SEO ID NO: 226

Sequence ID 626SEQ ID NO: 227

Sequence ID 627SEQ ID NO: 228

Sequence ID - 628 SEQ ID NO: 229

nt:

419

Sequence ID 629SEQ ID NO: 230

CTGAGAGTCACTGTGTTTTTAGCCAAATCTAAGGGAGAAAATGAATATTGATAGCA GCATGCTGTAGCCAGCTCCTTAAAGGAAGGATGGTGCCTGGTACAGAGTTAGAGTT AGTGCTTCAGTAAATAATGAATGTGTGCTAGGTAGGTTCTGCTGGGTAGGCTGCAT

Sequence ID-630SEQ ID NO: 231

Sequence ID 631SEQ ID NO: 232

TNCACTCACACACTCCCAAACCTTAACAAACACATACATGTGCAGCCAACCCAATG
GGCCAGCCTCTTTTATGCTCCTCACATGTTTCCTTTAACTGGAATACCCATGACAG
CTCCCTACATAGTTACTTGTAAACTCCTCCTCTCTGTATAAGTTTTCCTGAATTTT
TTTGATAAAATTAAGTTGTGCCACCCCTTTATGCTCTCTTANAACTTTGTTCTGTT
CTCATGGCTGTTCTGCAACGAATCTCATTGTGTTCTCTACTCAATTACATTCCTG
CGTCTCCCACTAGATGGCAGACTCTTTGAGAGTAGGAGATTCCCTTGTTATCTCTG
GATCCCTGGCACTTGCAGAAAGCCTGTTACGTAATAATTGCTCAACAATTAGTTTT
TAAATAAATGAATTATTTTTAAAACGCCAAAATTACAATGATTGTGCATTAAGTGA
AAGATGACCATCTAAAAACATAAAGCCATGCTTCATGACATTGGC

Sequence ID 632SEQ ID NO: 233

GACCATTCAGGGAAATTTTATAAAAAATGCAGATACTGTCTTGAGCAGATCGAAAT
GCCGATGAGGTGGATGCAATTTCCTTTTGTGCAAGCAGTGCACGGTGCCCCCCCT
CGGGTGTCCGTGCTGTGCCTTAGCTTCCCCAGGTGCCGGGACTCACACCTGCTAGG
GGCTGGGCAAGGCCCCGGCTCTGCTTTCTCTGAAGGGCTTGTCCAAGTTCATTGCC
CTGTTACAGGTGGTCAAGACGTCCGGCCGCCTTGACCCAGGCTACCCTTAGCCAAT

ATCCTCTGCCCCTGGGTGGTTGGTGGCCTGGGCCTCAGGGTGGGCAACGTTAGGGGT
TTGGCGAAAGCCCGCCCCATGGGATTGAGGGACGGGGCTGCACTCCAACCGTCTGC
ACCTGCTCTTCCCCCACCCCTGTGGGACCTCATCTTCACGTGCCATGTGTGCTGAA
GGCCCAGGGCCCAGCAGGGGGCAGTGGCACCTGTTGACGGAAAAGCCGAGGTGCTT
ACCAATGGACCTTCTGGCCCGCCCTCCCCTGTACTTGTCGGGCATTCAGGGCCCCG
ACCTGTGCCTACCCGCA

Sequence ID 633SEQ ID NO: 234

Sequence ID - 634SEQ ID NO: 235

nt:

511

Sequence ID - 635SEQ ID NO: 236

nt:

592

TGAGCGTTGGGCTGTAGGTCGCTGTGTGTGATCCCCCAGAGCCATGCCCGAGA

TAGTGGATACCTGTTCGTTGGCCTCTCCGGCTTCCGTCTGCCGGACCAAGCACCTG
CACCTGCGCTGCAGCGTCGACTTTACTCGCCGGACGCTGACCGGGACTGCTCT
CACGGTCCAGTCTCAGGAGGACAATCTGCGCAGCCTGGTTTTGGATACAAAGGACC
TTACAATAGAAAAAGTAGTGATCAATGGACAAGAAGTCAAATATGCTCTTGGAGAA
AGACAAAGTTACAAGGGATCGCCAATGGAAATCTCTCTTCCTATCGCTTTGAGCAA
AAATCAAGAAATTGTTATAGAAATTTCTTTTTGAGACCTCTCCAAAATCTTCTTCTGCTC
TCCAGTGGCTCACTCCTGAACAGACTTCTGGGAAGGAACACCCATATCTCTTTAGT
CAGTGCCAGGCCATCCACTGCAGAGCAATCCTTCCTTGTCAGGACACTCCTTCTGN
GAAATTAACCTATACTGCAGAGGTGTCTGTCCCTAAAGAACTGGTGGCACTTATGA
GTGCTATTCGTGATGGAGAAACACCTGACCCA

Sequence ID - 636SEQ ID NO: 237

nt:

572

Sequence ID - 637SEO ID NO: 238

nt:

482

Sequence ID - 638SEQ ID NO: 239

nt:

545

Sequence ID - 639SEQ ID NO: 240

nt:

624

Sequence ID 641SEQ ID NO: 241

CAAGATGACAAAGAAAAGAAGGAACAATGGTCGTGCCAAAAAAGGGCCGCGGCCACG
TGCAGCCTATTCGCTGCACTAACTGTGCCCGATGCGTGCCCAAGGACAAGGCCATT
AAGAAATTCGTCATTCGAAACATAGTGGAGGCCGCAGCAGTCAGGGACATTTCTGA
AGCGAGCGTCTTCGATGCCTATGTGCTTCCCAAGCTGTATGTGAAGCTACATTACT
GTGTGAGTTGTGCAATTCACAGCAAAGTAGTCAGGAATCGATCTCGTGAAGCCCGC
AAGGACCGAACACCCCCACCCCGATTTAGACCTGCGGGTGCTGCCCCACGTCCCC

Sequence ID 642SEQ ID NO: 242

Sequence ID 643SEQ ID NO: 243

Sequence ID 644SEQ ID NO: 244

ATGAGCCTGGTACTCGATAAATGGGGACTTNCTTAAAA

Sequence ID - 645SEQ ID NO: 245

nt:

649

CTACAGCCTGGGCAGCGCGCTGCGCCCCAGCACCAGCCGCAGCCTCTACGCCTCGT
CCCCGGGCGGCGTGTATGCCACGCGCTCCTCTGCCGTGCGCCTGCGGAGCAGCGTG
CCCGGGGTGCGGCTCCTGCAGGACTCGGTGGACTTCTCGCTGGCCGACGCCATCAA
CACCGAGTTCAAGAACACCCGCACCAACGAGAAGGTGGAGCTGCAGGAGCTGAATG
ACCGCTTCGCCAACTACATCGACAAGGTGCGCTTCCTGGAGCAGCAGAATAAGATC
CTGCTGGCCGAGCTCGAGCAGCTCAAGGGCCAAGGCAAGTCGCGCCTGGGGGACCT
CTACGAGGAGGAGATGCGGGAGCTGCGCCGGCAGGTGGACCAGCTAACCAACGACA
AAGCCCGCGTCGAGGTGGAGCGCGACAACCTGGCCGAGGACATCATGCGCCTCCGG
GAGAAATTGCAGGAGGAGATGCTTCAGAGAGAGGAAGCCGAAAACACCCTGCAATC
TTTCAGACAGGAAATCCAGGAGCTGCAGGCTCAGATTCAGGAACAGCATGTCCAAA
TCGATGTGGATGTTTCCAAGCCTGACCTCACGGCTGCCTTGCGTGACGTACCTANC
AATATGAAAGTGTGGCTGCCAAAAACCTTGCAG

Sequence ID - 646SEQ ID NO: 246

nt:

600

Sequence ID 647SEQ ID NO: 247

TGAGGTCTGTACGTTACCTCTTAACAATTTCTGTCCTTCAGATGGAAACTCTTTAA CTTCTCGTAAAAGTCATATACCTATATAATAAAGCTACTGATTTCCAAAAA

Sequence ID - 649SEQ ID NO: 249

nt:

425

Sequence ID 650SEQ ID NO: 250

Sequence ID - 651SEQ ID NO: 251

nt:

251

CTTTGGGAGGCCGAGGCGGATCACTTGAGGTCAGGGGTTCGAGACCAGTCTG GCCAACATGGTGAAACCCCAACTCTACTAAAAATACAAAAGTTAGCCAAGTGTGGT GGCAAGTGCCTGTAATCCCAGCTACTCGGGAGGCTGAGACAGGAGAATCACTTTGA

ACCTGGGAGGCGAGGTTGCAGTGAGCCAAGATCGTGCCACTGCACTTCAGCCTGGGCAACAGAGCAAGATTCCGTCCATCTC

Sequence ID 652SEQ ID NO: 252

Sequence ID 653SEQ ID NO: 253

Sequence ID 654SEQ ID NO: 254

GTTGCTAGTAGCGGCAGGAAGATGTCAGGCTCACTTTCCTCTGATTCCCGAAATGG
GGGGAACCTCTAACCATAAAGGAATGGTAGAACAGTCCATTCCTCGGATCAGAGAA
AAATGCAGACATGGTGTCACCTGGATTTTTTTCTGCCCATGAATGTTGCCAGTCAG
TACCTGTCCTCCTTGTTTCTCTATTTTTTGGTTATGAATGTTGGGGTTACCACCTGC
ATTTAGGGGAAAATTGTGTTCTG

Sequence ID 655SEQ ID NO: 255

Sequence ID 656SEQ ID NO: 256

TAGAGGCCTGAATAGGTAGACAATGGCAGCAGCGTTTTTAATCACAGTCCTATTCA
TGCCCTAATTCGGGAGTGATGATTAAAGGACATTAGAGGGAGCACTTTGACATCTG
ATCCTTTGAACTGACGTCTGTGCAGGCTGCACTCCATAGAGCTCACTTGGCCAAAC
TGATTTCCTTAAATAAAGTGCTGTGATTTCCAATGTAGGAAATATTACATTAGAGC
CTATTGAAATGATTAGGAATTGAGGAGCTTTTCTTTAGGTGGGAATGTGGTGTATG
CTGTATACTCACAAAAGTGAGATCATTAATATTTGCATGTACTACTTTGAATATCAG
GGACCACAGAGAAATAGCATGAGAAACGCCTTCCTGCAGTCATGCACTTAAAATGA
ATATGAACAAAAATGTGGAACTCTGCTGTCATAGCTCTCCG

Sequence ID-657SEQ ID NO: 257

Sequence ID 658SEQ ID NO: 258

Sequence ID 660SEQ ID NO: 259

Sequence ID 661SEQ ID NO: 260

CTCTGGCACACTTAGTTCCTCTTATATTACATTGATATAAGCAAGTCATATGGAT
TTATCTGAGTGTAAGGAGAGCTGGAAAAAATAGTTTCTAGCAGGTCAGCCACCTCC
CAGTGAGGGCTGCATACCATAGAAGGGGAGAATGAATTTTGGGAAAACAGGTAATT
ATCTCTGTCACAGAAGGGGATGAAAAGTATGGTAGTTACNCAAGTTANACATCTGT
ATGGAAAATACCACTTGGTTCTACAAATGNGG

Sequence ID - 663SEQ ID NO: 261

nt:

627

Sequence ID - 665SEQ ID NO: 262

nt:

345

ACCAGTAGACGCTCCTCTACTCTTTGAGACATCACTGGCCTATAATAAATGGGTTA
ATTTATGTA

Sequence ID - 666SEQ ID NO: 263

nt:

252

ATAATTCAGAACTTCTTCATATGCTCGAGTCTCCAGAGTCACTCCGTTCTAAGGTT
GATGAAGCTGTAGCTGTACTACAAGCCCACCAAGCTAAAGAGGCTGCCCAGAAAGC
AGTTAACAGTGCCACCGGTGTTCCAACTGTTTAAAATTGATCAGGGACCATGAAAA
GAAACTTGTGCTTCACCGAAGAAAAATATCTAAACATCGAAAAAACTTAAATATTAT
GGAAAAAAAAACATTGCAAAATATAAAAT

Sequence ID 669SEQ ID NO: 264

TTACTTTTAACCAGNGAAATTGACCTGCCCGTGAANAGGCGGGCNTGACACAGCAA
GACGAGAAGACCCTATGGAGCTTTAATTTATTAATGCAAACGGTACCTAACAAACC
CACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTCGGTTGGGGCGACCTCGGA
GCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTA
CTATACTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAAC
AGCGCAATCCTATT

Sequence ID 670SEQ ID NO: 265

Sequence ID 671SEQ ID NO: 266

Sequence ID 672SEQ ID NO: 267

Sequence ID 673SEQ ID NO: 268

Sequence ID 674SEQ ID NO: 269

ACCTCTAGCATCACCAGTATTAGAGGCACCGCCTGCCCAGTGACACATG-TTTAAC
GGCCGCGGTACCCTAACCGTGCAAAGGTAGCATAATCACTTGTTCCTTAATTAGGG
ACCTGTNTGAATGGCTCCACNAGGGTTCACTTGTCTCTTACTTTTAACCAGTGAAA
TTGACCTGCC

Sequence ID - 675SEQ ID NO: 270

nt:

591

GTATAGAAAATAATGTCCCCAGNGCATAGAAAAAATGAGTCTCTGGGCCAGTGAAT ACAAAACATCATGTCGAGAATCATTGGAAGATATACAGAGTTCGTATTTCAGCTTT

Sequence ID-676SEQ ID NO: 271

Sequence ID 679SEQ ID NO: 272

Sequence ID 682SEQ ID NO: 273

CACCTGCAGTCCAAGTACATCGGCACGGGCCACGCCGACACCAAGTGGGAGTGGCTGGTGAACCAACACCGCGACTCGTACTGCTCCTACATGGGCCACTTCGACCTTC

TCAACTACTTCGCCATTGCGGAGAATGAGAGCAAAGCGCGAGTCCGCTTCAACTTG
ATGGAAAAGATGCTTCAGCCTTGTGGACCGCCAGCCGACAAGCCCGAGGAAAACTG
AAACTTTGCTTAACNACCGAATGGNGGGGANCTTTTCCAACGNTTTT

Sequence ID 683SEQ ID NO: 274

TTGGTTTCATACTGNTGGGGNTTGAATGNTCCCTNCAACACTNATGTTGANACTTA
ATCCCTAATGNGGCAATACTGAAAGGTGGGGCCTTTGAGATGTGATTGGATCGTAA
GGCTGTGCCTTCATTCATGGGTTAATGGATTAATGGGTTATCACAGGAATGGGACT
GGTGGCTTTATAAGAAGAGGAAAAGAGAACTGAGCTTGCATGCCC

Sequence ID - 684 SEQ ID NO: 275

nt:

545

GTGGAAGNGACATCGTCTTTAAACCCTGCGTGGCAATCCCTGACGCACCGCCGTGA
TGCCCANGGAAGACAGGGCGACCTGGAAGTCCAACTACTTCCTTAAGATCATCCAA
CTATTGGATGATTATCCGAAATGTTTCATTGTGGGAGCAGACAATGTGGGCTCCAA
GCAGATGCAGCAGATCCGCATGTCCCTTCNCGGGAAGGCTGTGGTGCTGATGGGCA
AGAACACCATGATGCGCAAGGCCATCCGAGGGCACCTGGAAAACAACCCAGCTCTG
GAGAAACTGCTGCCTCATATCCGGGGGAATGTGGGCTTTTGTGTTCACCAAGGAGA
CCTCACTGANATCAGGGACATGTTGCTGGCCAATAAGGTGCCAGCTGCTCGGG
CTGGTGCCATTGCCCCATGTGAAGTCACTGTGCCAGCCCAGAACACTGGTCTCGGG
CCCGATAAGACCTCCTTTTTCCAGGCTTTAGGTATCACCACTAAAATCTCCAGGGG
CACCATTGAAATCCTGAGTGATGTGCACTGATCAAGACTGG

Sequence ID 685SEQ ID NO: 276

Sequence ID 686SEQ ID NO: 277

Sequence ID - 687SEQ ID NO: 278

nt:

268

Sequence ID - 688SEQ ID NO: 279

nt:

569

Sequence ID 689SEQ ID NO: 280

GCAATGCTTTTAGATTAAAATGAAGGTGACTTAAACAGCTTAAAGTTTAGTTTAAA
AGTTGTAGGTGATTAAAATAATTTGAAGGCGATCTTTTAAAAAAGAGATTAAACCGA
AGGTGATTAAAAGACCTTGAAATCCATGACGCAGGGAGAATTGC

Sequence ID 690SEQ ID NO: 281

CGAAAAGCAAATATAACTTGCCACTAACCAAGATCACCTCTGCAAAAAGAAATGAA
AACAACTTTTGGCAGGATTCTGTTTCATCTGACAGAATTCAGAAGCAGGAAAAAAA
GCCTTTTAAAAAATACCGAGAACATTAAAAATTCGCATTTGAAGAAATCAGCATTTC
TAACTGAAGTGAGCCAAAAGGAAAATTATGCTGGGGCAAAGTTTAGTGATCCACCT
TCTCCTAGTGTTCTTCCAAAGCCTCCTAGTCACTGGATGGGAAGCACTGTTGAAAA
TTCCAACCAAAACAGGGAGCTGATGGCAGTACACTTAAAAAACGCTCCTCAAAGTTC
AAACTTAGATTTCAGATTT

Sequence ID 691SEQ ID NO: 282

Sequence ID 692SEQ ID NO: 283

AATTCGNGGCCGCGTCNNCCTANGAGGCACCAGGAAATCCCGCGGGGTGGCCCATG
CAGACCAGGCGCACGTGGCTCATGGGGCANAATTGCCAAGGACAGCTCACGACAGT
GCCACCTTCTCACCATTCCAGCCAAGGAGAGATGTGACGTTGGAACTGCTCTGGCA
CTTCTGTCAAGCCTCCCCGCCCCAATTGCCTTGAGATCTCTGCTCTTTGTCAGAG
ATTTGCAAAGACTCACGTTTTTGTTGTTTTTCTCATCATTCCATTGTGATACTAAGA
AACTAAGAAGCTTAATGAAAAGAAATAAAATGCCTATGTTGTTGTTCT

Sequence ID 693SEQ ID NO: 284

CTAGAACCCATGACTCCTAGGTCTTATACTGCAACCACAGTATCAGCAAATAATCT
TTCATAAGGGGATTATTCTCTGATTAACAGGAAATACAGGAATTTAATTTGTGAAC
ACGCTAGGTAGAAGCAGAAACCCAAATCCAAATCCAAATTTAAACATTTAAAATTC
ATTCTATAACTAAGATCTAACAGTCATTTTCTTCCCAGTAAGAAATAACCAAAGCA
TGCTAAAAATCACTGGACTAAATTGGTGTCAAAACTGCCACATTGCCAGGCATGGG
GGGGTCATACTTGTAATCCCAGCACTTTGGGAGGCCGAGGTGGGAAAATTGCTTGA
GGCCAGGAGTTCGAAACCAGCCTGGGCAACACAGTGAGACCCCATCTCCACAAAAA
AAAAAAATTAAAAAACAAAAACAAAACATTAGCTGGGCATGGTGGTACACGCCTGTA
GTCCCAGCTACTCAGGAGCCTGAAGTGAGAGATCACTGAAGCCCAGGAGGTAGAG
CTATGACTGTAGTGAGCTATGACTGTGCCACTACACTCCACCTGGGTGACAGGGGA
CTC

Sequence ID 694SEQ ID NO: 285

Sequence ID 696SEQ ID NO: 286

Sequence ID 697SEQ ID NO: 287

GAACATTTAAAAATAATGCAAATAAGGCTGGGCGTGGGGGCTCACACCTGTAATCC
CAGCACTTTGGGAGGCCGAGGCAGGCAGATCACGAGGTCAGGAGATTGAGACCATC
CTGGCTAACACAGTGAAACCCTGTCTCTACTTAAAAAAATAAAAAATTAGCCAGGC

GTGGTGGTGGCCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGGAGAATGGT GTGAACCCGGGAGGCGGAGCTTGCANTGAGCTGAGATCGTGCCACTGCACTCCAGC CTGAGCGACAGAGCGAGACTCTGTCT

Sequence ID 698SEQ ID NO: 288

TCATTAGAATCCAAGCTTTGAAAATTTCTGATTAATGCTCATGTATTTCTTTATCT
TTGTTTTTCCTTGTGAAGAAAGACTTTCACCACTGTCTGAGTGATGATGCTGTTGA
TAAGGATGATGTCGATGACTACTATATTGCATCTCTCAGGAACAGCTGATGGGAAG
GGAGGGGCTGCTGAGTTCCCTTGTTCTAGCTAGCAGCACGCTCCTCANAGAGGGGG
CCGAGTTACAGACAGCAGCCGCATTCTCATGCAAAATTAGTTTTAAACTGCTAGTG
TGGGCATCGGTACCTTTTGCCTGGGTGATACCGAAGAATTGTTGAGGATTTAGTAT
GCTCCGTAGAGACAGTTCAGCCAGTCATTTCTGCATTGGAGAGACTTCTCATACTT
TCTTTGAAGACTCATAGAAAGCTGGAT

Sequence ID 699SEQ ID NO: 289

ATTAAGGTTTGTNCCCAACAAGAATAGATGTAATTAGAAAAAANTGNCTTCCTTAC
CTATTGCCTCTGATNTTTACTTGCTTAAATTTTTTTTTATTGNAAATCCAGAAAAAG
NGGATTTAGAGAACAACACTAACTCCCACCTAATCTATGACAGANATGTACAANAN
AGTACCTGTGAAAAATGTGAAAGNATNTGAAAAATGTAACCTTTGGCAGCCTGAGC
ATAGTCAACCAGAAAAACTATCTGAATTAAAATAATTGGTCCATAGGTACTATTTT
ATTTGGTCCATAAGGATTATTTTTTCAACTTTTTTTCAAGTGTATTATTATGTCA
TTTCCCACGTAGGTTACTGATACCTGAAGACTTTTTTNCACCTTTAACCTTNCTCGT
TGAGGAGCTTTGTANTCTAATAAAAAGAGAAATATAAGTAAATGTTAGATATATGGG
NGGATAATGGTAACTATGTGCTTAAAGAGGGTATAAAAAGAAGGGTAGGGAAGAAAAA
GACAAAGGAAGGGCTATATTATAANGAAGAATATTCCAAGTAGGGAAGAAAAA
GATATGTTATCCATATAATATTTTATGTGCAGTAGAGAACATGTTCTATAGAANAG
ACAGAAGATG

Sequence ID 700SEQ ID NO: 290

AGAGACACGCAGGAAGCAGGTGAACCATGAAGGGCCAACACATGCCCCCAGTTAGC
AGGGTGTAGAGACCGGGGCAGGGCTTTCTTCTTCTTCTTCTTGGGTTATAAATATCCAT
GTCCTGCCATTTGAAGCTGCAAGTGGCACACATGGATGCTGGACAGGCGCTCGCAC
TTTCTGGGCAGGCANGGGGCTCAAAGGCAGGACAGCTGGGCAAAAGCACCTTGCG
TGGGCCC

Sequence ID - 701SEQ ID NO: 291

nt:

579

Sequence ID 702SEQ ID NO: 292

GTNNTCCTCTCGGAACGCGCCTTNTGTAGCCAGGTGCTACCAGACCNAATACACGG
TTGTTCCAGCTTGCGCATTCACCGATGGCGTAGATATCCGGATCGGAAGTCTGGCA
GGAATCATTAATGACAATACCCCCACGCGGAGCAACGTCCAGACCACACTGGGTTG
CCAGCTTATCGCGCGGACGGATACCGGTAGAGAAGACGATAAAGTCGACTTCCAGT
TCGCTGCCGTCGGCAAAACGCATGGTTTTACGCGCTTCAACACCTTCCTGCACAAT
CTCAAGGGTGTTTTTGCTGGTGTAACGCGCACGCCCATACTTTCGATTTTGCGAC
GCAGCTGCTCGCCGCCCCATCTGATCAAGCTGTTCTGCCATCAGCATAGGGGCAAAT
TCGATAAC

GTGGGTTTCAATACCTAAGTTTTTCAGCGCGCCTGCGGCTTCCAGACCTAACAGGC
CGCAATTCGAGCTCGGCCGACTTGGCCAATTCGCCCTATAGTGAGTCGTATTACAA
TTCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAAC
TTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAAGAGGC
CCGCACCCGATCGCCCTTTCCAACAGTTGCGCACCTGAATGGCGAATGGAAATTGT
AAGCGTTAATATTTTGTTAAAATTCGCGT

Sequence ID 703SEQ ID NO: 293

Sequence ID 704SEQ ID NO: 294

Sequence ID 705SEQ ID NO: 295

Sequence ID - 707SEQ ID NO: 297

nt:

397

Sequence ID - 708SEQ ID NO: 298

nt:

293

CCAGCTTTTTATGGTGTTTAATCTAATACACTTAAGCTGCAGTCCCAAAATTAGGG GTCCTTCAGTCTTGGAGACTATAAGGGAGCCTCTGCACCCAGGGAAAATGTTACCC TTTACAGGGGGGAAGGGTAAACCAGTAGGGAATACAGTACAATCCCAACCCTACTG GGAGGGGCGGAGGGAGGTGTTGCCGTCACTGTATTAAGTCGATGTTGGGAAACGT TTTAACATCTGGAGCCTTTGTGGGTGGAAATATGTCTCCAGTTACAACTCCGCAGT GGATGTGAAGAAG

Sequence ID 709SEQ ID NO: 299

Sequence ID 710SEQ ID NO: 300

TGGATTCCCGTCGTAACTTAAAGGGAAACTTTCACAATGTCCGGAGCCCTTGATGT
CCTGCAAATGAAGGAGGAGGATGTCCTTAAGTTCCTTGCAGCAGGAACCCACTTAG
GTGGCACCAATCTTGACTTCCAGATGGAACAGTACATCTATAAAAGGAAAAGTGAT
GGCATCTATATCATAAATCTCAAGAGGACCTGGGAGAAGCTTCTGCTGGCAGCTCG
TGCAATTGTTGCCATTGAAAACCCTGCTGATGTCAGTGTTATATCCTCCAGGAATA
CTGGCCAGAGGGCTGTGCTGAAGTTTGCTGCTGCCACTGGAGCCACTCCAATTGCT
GGCCGCTTCACTCCTGGAACCTTCACTAACCAGATCCAGGCAGCCTTCCGGGAGCC
ACGGCTTCTTGTGGTTACTGACCCCAGGGCTGACCACCAGCCTCTCACGGAGGCAT
CTTATGTTAACCTACCTACCATTGCCCTGTGT

Sequence ID - 711SEQ ID NO: 301

nt:

498

GTGGTACATATACACAAAGGAAAACTATGTAGCCATTAAAAGAAAAGGAACTCCTA
TCATTTGTAACAACATAAATAAATCTGGAGGAGATTAGGCTAAGGTGAAATAAGCC
AGGCACAAAAAGACAACTACCATATGATCTTACTTATACGTGTGTGGAATCTAAAA
AGGTGGAATTTACAGAAGCAGAGAGTAGAATGGTGATTACCAGAGGCTGGGGAGTG
AGGGCAGGAGGTTGGAGAAATGTTGGTCAAAGGATACAAAGTTTCAGTTATACAGG
ATGAATAAGTTCAAGAGATCTATTGTACAACGTGGTGGCTATAGTTGATAACAATG
TATTGTGTTCTTGAAAAATGCTGAGAGAGTAGATTTTAAGTGTTCTCACCACAAAA
CATAAGTATGTGAGGTAATGCATGTGTTAATTANCTTAATTTAGACATTTCATAAT
GTATTATACATATTTCAAAACCACGTTGTACATGAGAAAGATACACAATT

Sequence ID 713SEQ ID NO: 302

CCTAGACAACTATACCCGATCGCATTCAGGTCCTTCGCAACATGGTCACTGTGCAG ACCTGAGCAACCCCACCAAGTCCTTG

Sequence ID 714SEQ ID NO: 303

Sequence ID 717SEQ ID NO: 304

Sequence ID 718SEQ ID NO: 305

AAGTGGNGGGCTTGCTTTGTGAAGAGACAGTTCATGAACAANAGTCTTTCAGGACC TGGACAGTGAAGGGAGCCCGGCCAGCCA

Sequence ID 719SEQ ID NO: 306

CGNGGCCGCGTNAACTTTTGATCGTCAGCTGGGGCTGGCAGGCACCTAAATGGGAA
GGGTGATAGCAGTGTGTTGGGGGGAGTTTAGGGAACGGTCCTCTACCGATAGAGGC
AGCANCTCATTGGAATTTCCTCCTGAAGTTGTCTTGCCCCTTGAATCCTGCAGGAA
GGCTGGCAAATGGCCATTTCCCTTCCACTTGAATAGAGACCCATAACTCAAGTATC
TGCCCTTAAGACACCACAGGACTGTTCTTCGCGGGCCCTGCCCCTGGATTTGGGAG
AGGCAGTCCANCTCACCCAACTAGGCTCTGCANGGGGACCANGAGGGATGGTTGT
GTCCACAGGACCAGCCAGACTGATGAGGGATGCGCAAGCATATTCTCACCACCTT
CTTTCACGTTTACAACANACCAGCNTTCCCTGTGTGGCAGGGGTTACATTGGTCAC
CGAGGACCTANAATCATGGAGTGCTCTGGGGATCCGGGCTTGGA

Sequence ID 720SEQ ID NO: 307

TCAGTGTTGAATTTTGTCAGACACTTTCTCTGCATCAATTGGTATGACCATGTGAT
TTTTTTTCTGTAGCCTGTTAATATGGTTAATTTTCAAATATTGAGCTGATTAATTT
TCAAATATTGAGCTCTCCTTGCATCTCTGGAATAAGTACCACTTGGTCGTGGTATA
TATTTCTTTTAATATATTGCTGAATTCTGTTTGATCATGTTTTCTTAAAGACTTTC
GTGTCTGTTTTCATGATAGATACTGGTCTATAGTTTTTGTTGTAATATCTTGGTTTG
ATTTTGATATCAGGATAATGCTACCTTAATAGAATGAATTGGAGCCAAGTATGGTG
GCAAATGCCTATAGTCCTAGCTACTCAGGAGGCTGAGGTGGTGGGGACTGCTTGAC
CCANGAGTTCAAATCTAGCTTGGGCAATGTAGCAAGAC

Sequence ID 721SEQ ID NO: 308

Sequence ID 722SEQ ID NO: 309

Sequence ID 724SEQ ID NO: 310

Sequence ID - 726SEQ ID NO: 311

nt:

260

CGGGGTCTGTACCGGGCTGGCCTGTGCCTATCACCTCTTATGCACACCTCCCACCC
CCTGTATTCCCACCCCTGGACTGGTGGCCCTGCCTTGGGGAAGGTCTCCCCATGT
GCCTGCACCAGGAGACAGACAGAGAAGGCAGCAGGCGGCCTTTGTTGCTCAGCAAG
GGGCTCTGCCCTCCCTCCTTCCTTGCTTCTCATAGCCCCGGTGTGCGGTGCAT
ACACCCCCACCTCCTGCAATAAAATAGTAGCATCGG

Sequence ID 727SEQ ID NO: 312

Sequence ID 728SEQ ID NO: 313

Sequence ID - 736SEQ ID NO: 314

nt:

641

Sequence ID 739SEQ ID NO: 315

Sequence ID 747SEQ ID NO: 316

CAGAGTGCAAGACGATGACTTGCAAAATGTCGCAGCTGGAACGCAACATAGAGACC
ATCATCAACACCTTCCACCAATACTCTGTGAAGCTGGGGCACCCAGACACCCTGAA
CCAGGGGGAATTCAAAGAGCTGGTGCGAAAAGATCTGCAAAAATTTTCTCAAGAAGG
AGAATAAGAATGAAAAGGTCATAGAACACATCATGGAGGACCTGGACACAAATGCA
GACAAGCAGCTGAGCTTCGAGGAGTTCATCATGCTGATGGCGAGGCTAACCTGGGC
CTCCCACGAGAAGATGCACGAGGGTGACGAGGGCCTGGCCACCACCATAAGCCAG
GCCTCGGGGAGGGCACCCCCTAAGACCACAGTGGCCAAGATCACAGTGGCCACGGC
CACGGCCACAGTCATGGTGGCCACGGCCACACCATAATCAGGAGGCCAC
CCTGCCTCTACCCAACCAGGGCCCCGGGGCCTGTTATGTCAAACTGTCTTGGCTGT
GGGGCTAGGGGCTGGGGCCAAATAAAGTCTCTTTCCTC

Sequence ID - 757<u>SEQ ID NO: 317</u> nt: 583

GAACCCTGCGGAGGGACTTCAATCACATCAATGTAGAACTCAGCCTTCTTGGAAAG
AAAAAAAAGAGGCTCCGGGTTGACAAATGGTGGGGTAACAGAAAGGAACTGGCTAC
CGTTCGGACTATTTGTAGTCATGTACAGAACATGATCAAGGGTGTTACACTGGGCT
TCCGTTACAAGATGAGGTCTGTGTATGCTCACTTCCCCATCAACGTTGTTATCCAG
GAGAATGGGTCTCTTGTTGAAATCCGAAATTTCTTGGGTGAAAAATACATCCGCAG
GGTTCGGATGAGACCAGGTGTTGCTTGTTCAGTATCTCAAGCCCAGAAAGATGAAT
TAATCCTTGAAGGAAATGACATTGAGCTTGTTTCAAATTCAGCGGCTTTGATTCAG
CAAGCCACAACAGTTAAAAACAAGGATATCAGGAAATTTTTTGGATGGTATCTATGT
CTCTGAAAAAAGGAACTGTTCAGCAGGCTGATGAATAAAGATCTAAGAGTTACCTGGC
TACAGAAAAAAGAACTGTTCAGCAGATGACACTTAAGACCTACTTGTGATATTTAAATGATG
CAATAAAAGACCTATTGATTTGG

Sequence ID - 764SEQ ID NO: 319

nt:

626

Sequence ID 766SEQ ID NO: 320

Sequence ID 768SEQ ID NO: 321

Sequence ID 773SEQ ID NO: 322

Sequence ID 776SEQ ID NO: 323

ACTTCTGTGAAGTACCCTTTGGCCCCTCGTTTTCAGCTCCTAAACTCACCTGGAAA
TAGATGTCAATCTAATTTTGGGTCTGACTAGTGCAGTAGGCATTTTTGGTGA

Sequence ID 782SEQ ID NO: 324

Sequence ID - 785SEQ ID NO: 325

nt:

556

CTTTTCTCTGGGTATAGATTTACCCTAGCACCTATCTCATTATATTGAATTTTCCA
GCATATTTAAATAAACTATTAATTAGTCACACTATCTTTAAAAAGTCACACTATCA
ACTAATCGTGACCGCAATTATCTAGGGGTGATAATCTGCTGAGTCTACTCTTTAAA
TACACTGGGACCCAGCATATTGAGTTATATTGGCACAGAAACTTCACTCTGGGTAT
AGATTTACCCTAGTACCTTGCCGGCAGGATCCTATTATTCATGGTTGTACAAGCAA
GGTTCAGGGAAGAGGCTGGCACAGAGAAGGTACCTGGTAACTGTTGTTTGAGGCTG
AATTCAGCTCAACTCAGCTCCAGTAGAGATGGTGTCCCCTTCTCTACCGTGTTGAG
ATAGTGTGCAGTCCCTTCCTAAGGGCTGTTACCCCACCGCAATAGGACTTGTCAGCT
TCAACTTTTAAATTTCTCTGCTCCCGCTGGGACCCACCCGCTTCAAAAATCATCAT
GGNGGNTTTAGCACCAATTTAGTAAACACAAACTGTCTGAAATATTTTTGGAT

Sequence ID 796SEO ID NO: 326

GAACATTCAAGATAGTGAGAGGAAGAAAAAGATATGGCTGTACGGGACCGAGGTCT
CTTCTATTATCGCCTCCTCTTAGTTGGCATTGATGAAGTTAAGCGGATTCTGTGTA
GCCCTAAATCTGACCCTACTCTTGGACTTTTTGGAGGATCCGGCAGAAAGACCTGTG
AATAGCTGGGCCTCAGACTTCAACACACTGGTGCCAGTGTATGGCAAAGCCCACTG
GGCAACTATCTCTAAATGCCAGGGGGCAGAGCGTTGTGACCCAGAGCTTCCTAAAA
CTTCATCCTTTGCCGCATCAGGACCCTTGATTCCTGAAGAGAACAAGGAGAGGGTA
CAAGAACTCCCTGATTCTGGAGCCCTCATGCTAGTCCCCAATCGCCAGCTTACTGC
TGATTATTTTGAGAAAACTTGGCTTAGCCTTAAAGTTGCTCATCAGCAAGTGTTGC
CTTGGCGGGGGAGAATTCCATCCTGACACCCTCCAGATGGCTCTTCAAGTAGTGAAC
ATCCAGACCATCGCAATGAGTAGGGCTGGGTCTCGGCCATGGAAAGCATACCTCAG

TGCTCANGATGATACTGGCTGTCTGTTCTTAACAGAACTGCTATTGGAGCCTGGAA
ACTCAGAATGCAGATCTTTTGTGAACAAAATGAAGCAAGAACCGGAGACNCTGAAT
AGTTTTATTTCTGTATTAAAAACTGNGATTGGAACAATTGAAGA

Sequence ID 801SEQ ID NO: 327

CCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAATAAAGTAT
AGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGATGA
AAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAAT
GAATTAACTAGAAATGAGGATTCTGACCTTGACTTTGATATCAGCAAATTGGAACA
GCAGAGCAAGGTGCAAAACACAGGACATGGAAAACCAAGAGAAAAGTCCATAATAG
ACGAGAAATTCTTCCAACTCTCTGAAATGGAGGCTTATTTAGAAAACAGAGAAAAA
GAAGAGGAACGAAAAGATGATAATGATGATGATGATGAAGACATAGCAAGTGATC
ATGATGATGAGCTGGGTTCAAACAAGATGATGAAATTGCTGAAGAAGAAGAAGAGAAGA
AAGGAAGCATTTCTGAAATATGAATGAAAAAAATTACATCTTTAGAAAAAAGAGTTA
TTAGAAAAAAAGCCTTGGCAGCCGTCNGGGGGAAGTGACGCACAGAAGAGACCAGAG
AATAGCTTCCTGGANGAGACCCTGCACTTTACCCATGCTGCTGGATGG

Sequence ID - 808 SEQ ID NO: 328

nt:

641

Sequence ID - 814SEQ ID NO: 329

nt:

132

Sequence ID 817SEQ ID NO: 330

Sequence ID - 821 SEQ ID NO: 331

nt:

370

AAAGAGCTCCCAAATGCTATATCTATTCAGGGGCTCTCAAGAACAATGGAATATCA
TCCTGATTTANAAAATTTGGATGAAGATGGATATACTCAATTACACTTCGACTCTC
AAAGCAATACCAGGATAGCTGTTGTTTCANAGAAAGGATCGTGTGCTGCATCTCCT
CCTTGGCGCCTCATTGCTGTAATTTTGGGAATCCTATGCTTGGTAATACTGGTGAT
AGCTGTGGTCCTGGGTACCATGGCTGGTTTCAAAGCTGTGGAATTCAAAGGATAAA
TTAATGAAGAAAACAAGCGGAGCTGAAGAAGAAAGTACAATATGGTGCTGTCTTCC
TAATGAAATAAATTCACTAAATGGACATTAAAAA

Sequence ID 825SEQ ID NO: 332

AGACTCGAGCAAGCTTATGCATGCATGCGGCCGCAATTCGAGCTCGGCCACTTGGC
CAATTCGCCCTATAGTGAGTCGTATTACAATTCACTGGCCGTCGTTTTACAACGTC
GTGACTGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCT
TTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTT
GCGCAGCCTGAATGGCGAATGGAAATTGTAAGCGTTAATATTTTTGTTAAAATTCGC
GTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAA
TCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGG
AACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGT

Sequence ID 833SEQ ID NO: 333

Sequence ID - 837SEQ ID NO: 334

nt:

603

TGAGGNTGGTCATGATGCANAAGCTACTCAAATGCAGTCGGCTTGTCCTGGCTCTT
GCCCTCATCCTGGTTCTGGAATCCTCAGTTCAAGGTTATCCTACGCGGAGAGCCAG
GTACCAATGGGTGCGCTGCAATCCAGACAGTAATTCTGCAAACTGCCTTGAAGAAA
AAGGACCAATGTTCGAACTACTTCCAGGTGAATCCAACAAGATCCCCCGTCTGAGG
ACTGACCTTTTTCCAAAGACGAGAATCCAGGACTTGAATCGTATCTTCCCACTTTC
TGAGGACTACTCTGGATCAGGCTTCGGCTCCGGCTCCGGCTCTGGATCAGGATCTG
GGAGTGGCTTCCTAACGGAAATGGAACAGGATTACCAACTAGTAGACGAAAGTGAT
GCTTTCCATGACAACCTTAGGTCTCTTGACAGGAATCTGCCCTCAGACAGCCAGGA
CTTGGGTCAACATGGATTAGAAGAGGATTTTATGTTATAAAAAGAGGATTTTCCCAC
CTTGACACCAGGCAATGTAGTTAGCATATTTTTATGTACCATGGNTATATGATTAAT
CTTGGGACAAGAATTTTATAGAAATTTTTAAACATCTGAAAA

Sequence ID - 839SEQ ID NO: 335

nt:

622

71

AAAAAAAAAAAAA

Sqeuence 849SEQ ID NO: 336

TTTTTTTTTTTTTTGAGAATGGAGTCTTGCTCTGCCGTCCAGGCTAGAGTTCAG

nt:

TGGTGCGATCTCAGCTCACCTGCCACCTCCTAGGTTCCAGAGATTCTTGTGC TTCAGCCTCCTCAGTAGTTGAGAATACAGGAACACGCCACCACGCCTAGCTAATTT TTGTATTTTTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCTGGTCTCAAACTC CTGGCCTAAGTGACCCACCTGCCTCAGCCTCCCAAAGTGCTGGGATTATAGGCGTG AGTCATTGTCCCCAGCCGGATGTTTTCATCTTGATTTGCCTTAGTTTCTAAATCTC ATCCTCTCCATTTTCTCCTGTTAGTAGTCACAGAGAACCAAATTCTGTCAAGTTAT GAAACTAAAGTCTCTCTCCACAAGTCTTCCTGTGTTCTGCCTCAAGTGAACTTGA AAGAACATCAGTTTGTGGGAAGGTTGAAGACCGAATGATCTGCTGGGAAATCACTG AGGCATTGCCATTCTCTTGAGGAATTTCATTTCATCGAAGTTTCGGTTTATATCC NTGAGC

Sequence ID - 860SEQ ID NO: 337

nt:

501

TCAAGATTTCATAATCATTTTTAGTATTTAGATTGTGCCTCAAAGTTGTAGTACCT CACAATACCTCCACTGGTTTCCTGTTGTAAAAACCTTCAGTGAGTTTGACCATTGT GCTCTTGGCTCTTGGGCTGGAGTACCGTGGTGAGGGAGTAAACACTAGAAGTCTTT AGTACAAAACTGCTCTAGGGACACCTGGTGATTCCTACACAAGTGATGTTTATATT TCTCATAAAGAGTCTTCCCTATCCCAAGGTCTTCATGATGCCAGTAGCCATATATG ATAAATTATGTTCAGTGATAACTTAGTTATCAGAAATCAGCTCAGTGGTCTTCCCC GCCATGATTCACATTTGATGAGTTTTTTAAAAATCAAAGTGATTTTTGAAAATCTCTA ATGGCTCAGAAAATAAAAACATCCAGTTTGTGGATGACTATATTTAGATTTCT

Sequence ID 864SEQ ID NO: 338

TTGTGTTTTTAGGACTCCTTATCTAAATTAAGGCAGAGAAGTTACAGTATTTATAT CTGCATTAAATCTCAATTCCAGAAAAACCTTTTGAAAAATTATTTAATCCTCTGGA AACTATTGATATGATACAGGAGAAATTTTCAGAAGTTTATTGAATAATTTAATATC ATTTAATAGGACACTCTGGCTTGTATATAAGCAGATACGTTACTCAGACTTCTTGG

CTGTACTCTAAAATAATATATGTACTAGTCTCCTAAATATTACTAGCTCACCTTTC
AAAATGCATACTAATATTTCAATGTCTTTCTTCAATTTGAAAAGCTCTTGAATATC
TACTTGTGATAGCCCTAAGAGCTGAGATAATTATTTTCCAGGAGGTTGAATCCCTGA
TTCTTAACTGTTCAGCAATGCATAAGCAAGAGAGAATATGACATAAGAGGACCATT
TCTACATTAGCCATTTTTTTTCACAAGATACCTATGTGAATACAGGGCACCTGGGA
GGGTAAGTGGAGGACTATTTCTAACTATATTTATAAGCACATACTGATATTGGTGA
ATCAAAACCTACAGCAGTGCTTCTCAGATGGGAAGGGAGACAATGTGTAAGGAGAT
CAGGAATTCATTAG

Sequence ID - 865SEQ ID NO: 339

nt:

122

Sequence ID 867SEQ ID NO: 340

Sequence ID - 869SEQ ID NO: 341

nt:

667

AAAATGCATACTAATATTTCAATGTCTTTCTTCAATTTGAAAAGCTCTTGAATATC
TACTTGTGATAGCCCTAAGAGCTGAGATAATTATTTCCAGGAGGTTGAATCCCTGA
TTCTTAACTGTTCAGCAATGCATAAGCAAGAGAGAATATGACATAAGAGGACCATT
TCTACATTAGCCATTTTTTTTCACAAGATACCTATGTGAATACAGGGCACCTGGGA
NGGTAAGTGGAGGACTATTTCTAACTATATTTATAAGCACATACTGATATTGNTGA
ATCAAAACCTACAGCAGTGCTTCTCAGATGGGAAGGGAGACAATGTGTAAGGAGAT
CAGGAATTCATTAGTCACCTTTCAGATGGTTTAATGCATACAGCTGTACCG

Sequence ID 870SEQ ID NO: 342

GGAGTTTGAGCAGATCCTTCAGGAGCGGAATGAACTCAAAGCCAAAGTGTTCCTGC
TCAAGGAGGAACTGGCCTACTTCCAGCGGGAGCTGCTCACAGACCACCGGGTCCCC
GGCCTTCTGCTCGAGGCCATGAAGGTGGCTGTCCGGAAGCAGCGGAAGAAGATCAA
GGCCAAGATGTTAGGGACACCAGAGGAAGCAGAGAGAGCAGTGAGGATGAGGCC
CATGGATCCTGCTCTCCGATGACAAGGGAGACCATCCCCCACCCCCGGAGTCCAAA
ATACAGAGTTTCTTTGGCCTATGGTATCGGGGTAAAGCTGAATCCTCTGAGGATGA
GACCAGCAGCCCTGCACCCAGCAAGCTAGGGGGAGAAGAGAGGAGGCCCAACCACGT
CTCCAGCTCCTGATCCGCCCTGTTCTGCCCTCCACGAACACCTTTGTCTGGGGGCC
TCAGCCGCCCCAGAGGCCTGACTTAGGGGTCTGGCTGTGGAAGGATGTTGTCCCC
AAATGAGGACAGGGCTCCCGCCTTCACAGCCCTCGCCAGGGGTCTGCCCCAATCCT
GGCCTGCATCAGGCAAGGACGGGGTCTCACC

Sequence ID - 871 SEQ ID NO: 343

nt:

642

Sequence ID 873SEQ ID NO: 344

Sequence ID 875SEQ ID NO: 345

Sequence ID - 876SEQ ID NO: 346

nt:

115

Sequence ID - 878SEQ ID NO: 347

nt:

Sequence ID 879SEQ ID NO: 348

Sequence ID 881SEQ ID NO: 349

TCGACTCTGATTTTTTTTCTCCTTCCTCGCAGCCGCGCCAGGGAGCTCGCGGNGC
GCGGCCCTGTCCTCCGGCCCGAGATGAATCCTGCGGCAGAAGCCGAGTTCAACAT
CCTCCTGGCCACCGACTCCTACAAGGTTACTCACTATAAACAATATCCACCCAACA
CAAGCAAAGTTTATTCCTACTTTGAATGCCGTGAAAAGAAGACAGAAAACTCCAAA
TTAAGGAAGGTGAAATATGAGGAAACAGTATTTTATGGGTTGCAGTACATTCTTAA
TAAGTACTTAAAAGGTAAAGTAGTAACCAAAGAGAAAATCCAGGAAGCCAAAGATG
TCTACAAAGAACATTTCCAAGATGATGTCTTTAATGAAAAGGGATGGAACTACATT
CTTGAGAAGTATGATGGGCATCTTCCAATANAAATAAAAGCTGTTCCTGAGGGCTT
TGTCATTCCCAGAGGAAATGTTCTCTTCACGGTGGAAAACACAGATCCAAGATGT

Sequence ID 883SEQ ID NO: 350

Sequence ID 885SEQ ID NO: 351

Sequence ID 887SEQ ID NO: 352

Sequence ID 889SEQ ID NO: 353

CAGAGAGCTTGTTCCCTCCCTGTGCATGCAAACAAGAGGGCATGGGAGCACA

Sequence ID 890SEQ ID NO: 354

Sequence ID - 891 SEQ ID NO: 355

nt:

626

AAATATCTNTACAACAAGAACTACAAAACTGCTGAAAAAAAATAGAGACACGCAAA
TAAGTAAAAAGGCACTCCATGCTCATGAATTTAAAGAATCAATATAATTAAAATGT
CCGNGCTGCCTAAAGCAACTTACAGATTAAAGGCTATTTCTCTCAAACTATAAATG
CACCTTTTA

Sequence ID - 893SEQ ID NO: 356

nt:

585

GTCATTGCTGGGTGGCGCCAGCCCTCAGACTTGCCTCTTTGCAGTAGGAAGAAGGC
CTCCCCACATACCTTCCCACACTCATCACCTTAAGCCAGACTCGGTGTCCAGTGAA
TATGACCATCTCTTGCCCATTTTCTAATGAGTGTTTTCATTAATGAGTTATAAGAA
TGTGGTGGGTAAATCTATGGGCTTTGAACTAGTGAATCAACTTGGTTTCAGAATCT
GGCACTGCTACTTACTAGTGAATTTAAGCAAGTTATTTCACCTTTCAGAGTGTCAG
TTCCCTCATGCATACAAGGAAGATAAAAAAATAATGTNTACNAAAGTATTGGAGTAA
TTAATACATGGAGAACTACATGTAAAGCGTTTAGCATGATGTCTGACATATTAAGC
ATCCAATATTAGTNGCTTGCAGAATTATTAGTAAAAGAGATTGCTTCTGAAAGCCA
TTCCAATTCTTAAATTTTATAATGCCACATTTGAGGTCACCTGAAGTCGTGTATAA
CATGTGTACATTTTTGCGATTTATTTTTTCAATTCCCANATTAAAGGCATAGAGAT
ATCCTAGCNANGGACTCCAAGTGTG

Sequence ID - 895SEQ ID NO: 357

nt:

560

Sequence ID 896SEQ ID NO: 358

Sequence ID - 897 SEQ ID NO: 359

nt:

509

Sequence ID 898SEQ ID NO: 360

Sequence ID 899SEQ ID NO: 361

Sequence ID 900SEQ ID NO: 362

Sequence ID 903SEQ ID NO: 363

GGAAACATAAGCTTGTTTCAGTACACTCACGCTGTAGATTAATTCTGATATTACAT
ATCTCCATCAGACTTTGTACCCTCTCTCTCTCCATCCCTTACCCTTACCGATTAGGT
TGGTATTACCTAAAAATCCATAGAAAATGTCCAGGTGAATTGCCTTATGCTTTCTA
CCCCATAAGGTATAATT

Sequence ID 904SEQ ID NO: 364

Sequence ID - 905 SEQ ID NO: 365

nt:

655

Sequence ID 906SEQ ID NO: 366

Sequence ID - 907 SEQ ID NO: 367

nt:

582

Sequence ID 908SEQ ID NO: 368

ACCTGACTTCAAACTATACTACGAGGCTACAGTAATCAAAACAGCATGGTACTAGT
ACAAAAACAGACCAATGGAACAGAATAGAGATCTCAGAAATAAAACTGCACATCTA
CAACCATCTGATCTTCAACAAACCTGACAAAACGAGCAATGGGGAAAGGATTCCCT
ATTTAATAAATGGTGCTGGGAGAACTGGCT-AGCCATGTGCAGAAAATTGAAACTG
GACCCCTTCCTTACACCTTATACAAAAATTAACTCAAGATGGATTAAAAACCCTTAGAACCCAAAAACGATAAAAACCCTAGAAGAAAATCTAGGCAATATCATTAAGG
ACATAGACCCAAAACGATAAAAACCCTAGAAGAAAACTCAAAAAGCAATGGCAACAAAA
GCAGAAACTGACAAATGGGCTTCTGCACAGCAAAAAGAAACTATCGTCAGAGTGAAC
AGACAACCTACAGAATGGGAGACAGTTTTTGCAATCTATCCATCTGACAAAAGTCT
AATATCCAGAATCTACAAGGAATTTAA

Sequence ID 910SEQ ID NO: 369

Sequence ID - 911 SEQ ID NO: 370

nt:

595

GCTGAGGATTGTAGAGCCATATATTGCATGGGGGTACCCCAATCTGAAGTCAGTAA
ATGAACTAATCTACAAGCGTGGTTATGGCAAAATCAATAAGAAGCGAATTGCTTTG
ACAGATAACGCTTTGATTGCTCGATCTCTTGGTAAATACNGCATCATCTGCATGGA
GGATTTGATTCATGAGATCTATACTGTTGGAAAAC

Sequence ID - 912SEQ ID NO: 371

nt:

651

CATTTCCAGAGTTTATGTGAATTGAATTGAACTATGGTTTTATGTTACTGTCAGTA
GAATGAAGTACGAATATTTGAAAAATACACCTTCAACTTCAAAGTGATTCTTGACA
AAAATTATAAGGAATCATTTTGGACACATTTTCTGGTAGAGCCTTGTAAAAATTAA
AACCAAGTGTTGTTTTCAAGAAGAACTGTAATACATAATCAGGAATTTGAGTAGGG
AGATTATTTTGTTATTTAAAATTAAAGTGGCTGTGTAGTTTTAACTTTAGTATTGC
AGGTAGAGTAAGCTTACATGATAACAAAAATCTTGGTCTTAGTGACTTAATGATTC
TGATATTTATTGATTGATTGGTTATCATTCCAAATATTTTAAAAGATAATAGCTGG
CTGGGTGCGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCCAGGACGGGCG
GATCACGAGGTCAGGAGATCAAGACCATCCTGGCTAACACGGTGAAACCCCGTCTC
TACTAAAAATCAAAAAATTAGCCGGGTGTAGTGGCGGGCACCTGTAGTCCCAGCTA
CTCAGGAGGCTGAGGCAGGAGAATGGCATGAACCTGGGAGGCGGAGCTTGCAGTGA
GCTGAAATCGTGCCACTGCCTCCACCTGGCGACAA

Sequence ID 913SEQ ID NO: 372

Sequence ID 914SEQ ID NO: 373

GGCGCCTGCTGGAGGAGAGAGAGCTCTGCTGGCATGAGCCACAGTTTCTTGACTG
GAGGCCATCAACCCTCTTGGTTGAGGCCTTGTTCTGAGCCCTGACATGTGCTTGGG
CACTGGTGGGCCTGGGCTTCTGAGGTGGCCTCCTGCCCTGATCAGGGACCCTCCCC

GCTTTCCTGGGCCTCTCAGTTGAACAAAGCAGCAAAACAAAGGCAGTTTTATATGA
AAGATTANAAGCCTGGAATAATCAGGCTTTTTTAAATGATGTAATTCCCACTGTAAT
AGCATAGGGATTTTGGAAGCAGCTGCTGGTGGCTTGGGACATCAGTGGGGCCAAGG
GTTCTCTGTCCCTGGTTCAACTGTGATTTGGCTTTCCCGTGTCTTTCCTGGTGATG
CCTTGTTTGGGGTTCTGTGGGTTTGGGTGGGAAGAGGGCCATCTGCCTGAATGTAA
CCTGCTAGCTCTCCGAAGCCCTGCGGGCCTGCTTGTGTGAACCGTGTGGACAGTGG
TGGCCGCGCTGTGCCTCGTGTTGCCTACATGTCCCTGGCTGTTGAGGCGCTGC
TTTAACCTGCACCCCTNCCTTG-CTCATANATGCTCCTTTTGA

Sequence ID - 915SEQ ID NO: 374

nt:

230

Sequence ID 917SEQ ID NO: 375

NNCAGATTTTTTTTTTTTTTTTCAGNGTTAGACCATCTTTCAATTCCTGGAACAAAC
TTAACTTTCCATGATATGTATTTTTTATACATTGCTGGATTTTATTTTGCTAATATT
TTACTTAGGATTTAATTTTCTAAGTNGACCTATAATTNTCCTGTATAAAATTGCAT
TTGTCACATTTTAGTATCAAGGTTGTCCTANCNCCATGAAATGGATTTANAATGGT
TTATGTAANATAAAGTACATTTCTTCTAAAGGTTTGNGTGGATTAACTTTCAAATC
TGCCANAGNGNGTTTTTTTCCTTTTTTTTTTTTTTTTTCATTTNAAGGGAGNGCAAGT
ANCTTTTCAAATNCTGATTTAATTTTTAAAATATTTNCAAGTNTNTTTANAGTTTT
TATTTNTTNTNGAANGTTAACATTTTTATANAAAANGGTNTTATCTTTTTAAATTC
TTTTGACATCAGTTTCTTCANAATTCCTTCTTTTAA

Sequence ID 926SEQ ID NO: 376

CCTTGATGGTTGTGGGGTCCTGATTTCAGCATTCATGAGTCAGGGGAAGG
TCCCTGCTAAGGACAGACCTTAGGAGGGCAGTTGGTCCAGGACCCACACTTGCTTT
CCTCGTGTTTCCTGATCCTGCCTTGGGTCTGTAG

Sequence ID 938SEQ ID NO: 377

Sequence ID - 939SEQ ID NO: 378

nt:

513

Sequence ID 947SEQ ID NO: 379

GAGAGTGAAAAAATTCTGGTACAAATTGGGAAATTAGTATATAACAACATAGTGTT
AAATTCAATGGGAAAAGTTTAATAAGAGGATTTGGTATCAACTGGCTGTCCAAAGA
TAAAAATGGACCGTCCTATCACATACAAAATTGTTTTTTTAGATAAAGATTTAAATA
CAGGCACTCCTTCATTTGCGTGGTGCACCTTGAGGTGTTGCAGAAATGATGAGAGC
TGAAACTGCAAAGCAATTTTAATACTTTATCTGTTGGAAATCTTATAGTTTTCCTG
TGACCGTTAAAATTTTCATTAAACTATTAAAAACACCCATGACTGGTCACAAATGT
ATTGGGAAATGGAAAAGAATTAATACACTAAAAAATACAAAAAATAGAAAATTTTA
AAATTATCTAAAAATTTGAAACATTAGAAAAATTGAGAACTAGGCAGGGCGTGGTG

GCTCACATCTGTAATTTTAGCCCTTTGGGAGGCTGANGCAGGTGGATCACCTGANG
TCAGGAGTTCGAGACCAGCCTGCCAACGTGGGGAAACCCCGTCTCTACTGAAAATA
CAAAAATTANCCGGGCATGGTGGCACAAGCCTGTAATNCTTGCTNACCAGGANGCT
GAGGCAGGAGAATCACTTGAACCCANGANG

Sequence ID 949SEQ ID NO: 380

GTTTCACATGAGAAGGTAGTATTATGTACAGTGACCTTGTTTAAAGTGTCNGTTTA
ATGTTACCACTAAGGCCCTGCCCCAGCTTTATCACCTGAGCACTAACAAGTGCTGT
GTGGAGTTCAGTCCATGCTGGTAACTNTTGAGTATTCAGTGGGTCTTTTAACAATT
ACCACCGTGGAGGANANAGCAAGGAAGAGAAATGCTGTGATCTTTTNCTGTTTTTA
ATTAGNGAAAGAGGGATTANATTAAACAAATGTTACAGAGNTGTGACTNTGATCCC
CCAGNGGTAAGCAATAATTGTANAGACTGGATTTNANAAGCCCTGAGAGTTTATTT
TCAACCTATNTATTATAGNNCAATCC

Sequence ID 1028SEQ ID NO: 381

ACAAGGCTTGGGGGCTGGACTCCCTCTACTGCCTCTGGCCATACCCCCTCCTGGAG ATGGGGTCAAGGCACCAGGACTGA

Sequence ID - 1056SEQ ID NO: 382

nt:

435

Sequence ID 1071SEQ ID NO: 383

NGATATAGTNCCGCATGGGAAAGATGANCAGGTATAACCNAGCNTNATATAGCAAG
GACTAACCCCCCTGCCTTCTGCATAATGAATTAACTAGAAATAACTTNGCAAGGAG
AGCCAAAGCTAAGACCCCNGAAACCAGACGAGCTACCTAAGAACAGNTAAAAGAGC
ACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTATAGGTAGAGGCGACAAACCT
ACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTAGTTCAACTTTAAATT
NGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAGTCCAAAGAGAGA

CAGCTCTTTGGACACTAGGAAAAACCTTGTAGAGAGAGTAAAAAATTTAACACCC
ATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACCCACT
ACCTAAAAAATCCCAAACATATAACTGAACTCCTNACACCCAATTGGACCAATCTA
TCACCCTATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGC
ATAAGCCTGCN

Sequence ID - 1074SEQ ID NO: 384

nt:

689

Sequence ID 1081SEQ ID NO: 385

Sequence ID - 1083 SEQ ID NO: 386

nt:

Sequence ID - 1084SEQ ID NO: 387

nt:

198

Sequence ID - 1099SEQ ID NO: 388

nt:

561

Sequence ID 1109SEQ ID NO: 389

TTTGNCGGTNTTGGANNNNNANAANTTTCTTCCANNCNTNACNTNTTGGTGGNCTA
AATTAANATGGNTTTNGNGGGTTCNTTNCTNNNTNNNNCATGGGANANAATTNATT
NTCNTNCNNNTTCCTTNNCCCTNAANCTACCTTCCCCCNATTTTCTCCCCTNTTCN
TNAATTANCATCCTCTCCNCNTANNTCNANACNTTAATGGCAANACTATCTAATAN
CNANNATAANANCTCCTGTNNNCCACATNTCTTATTNNNCGCNNCANGTTNCANNC
CCNCAGAGTNAACTCATCCTCNNCNNAANTTCATATCGTGNNCTNTNNNCNNTNGC
GCGANATATTAANNANACCNGTANNTNNNANACANNANNTNNGNAANAANCCTTCT
NANNTTTTAGCNTCNNGCNNTAACNNNNNTCTTNGTGNNNNCNCAGCTTTCNCNNC
ATNATNCTNCNNCGAANTNTCANNCNTCTCCNCTTNAATGNNTTCCCATGNATTAA

NTNCCTCGNNNANAGCACTATCGTNNNNGAGNNNATTATNGNCNNTTTACNTCATG
TGGTCCANTNNCGTTNGNCGCNNNNAATNTTCGTNNNNCNN

Sequence ID 1118SEQ ID NO: 390

Sequence ID 1125SEQ ID NO: 391

NGACTGGCTCCCGAAAAGAAGGGTGGCGAGAANAAAAAGGGCCGTTCTGCCATGGA
CGAAGTGGTAACCCGCGAATACACCATCAACATTNACAAGCGCATCCATGGAGTGG
GCTTCAAGAANCGTGCACCTCGGGCACTCAAAGAGATTCGGAAATTTGCCATGAAG
GAGATGGGAACTCCATATGTGCGCATTGACACCAGGCTCAACAAANCTGTCTGGGC
CAAAGGAATAAGGAATGTGCCATACCGAATCCGTGTGCGGCTGTCCANAAAAACGTA
ATGAGGATGAAGATTCACCAAATAAGCTNTATACTTTGGTTACCTATGTACCTGTT
ACCACTTTCAAAAAATCTACAGACAGTCAATGTGGATGANAACNAATCGCTGATCGT
CAGATCAAANAAANT

Sequence ID - 1139SEQ ID NO: 392

nt:

503

TATTGTGTTGTGCAGCATTAAAAAAATCAAAATAAAAATTAAATGTGAGCAAAG

Sequence ID - 1148SEQ ID NO: 393

nt:

587

Sequence ID - 1160SEQ ID NO: 394

nt:

650

Sequence ID - 1165SEQ ID NO: 395

nt:

502

CTCAAGTGAATCCTGGCTTCTTGGAAGCGCTTGCCTAGACGAGACACAGTGCATAA
AAACAACTTTTGGGGGACAGGTATGTTTTCTTGCAGCTGCGGTTGTAAGGTCTTGG
CAAGACAAGCAGTGTGGCCAGAATTTTGAACTTCTGATGAATGTGTAATGCAAAGG

Sequence ID - 1172SEQ ID NO: 396

nt:

648

Sequence ID 1178SEQ ID NO: 397

Sequence ID - 1180 SEQ ID NO: 398

nt:

622

CTTTTCCTCCCGCTGTCCCCCACGGGAGGGGACTGCTCTCCCCCGCTGCATCCTTT
CTGTGAGGTACCTTACCCACCTCAGCACCTGAGAGGGTGAAATAGAATTCTAACCT
CGACATTCGGGAAGTGTTTTTGAGAAGTCTCGGTCGGTAAGGGAAGTCTTCCAAGT
CCGTGCAGCACTAACGTATTGGCACCTGCCTCCTCTTCGGCCACCCCCCAGATGAG
GCAGCTGTGACTGTGTCAAGGGAAGCCACGACTCTGACCATAGTCTTCTCTCAGCT
TCCACTGCCGTCTCCACAGGAAACCCAGAAGTTCTGTGAACAAGTCCATGCTGCCA
TCAAGGCATTTATTGCAGTGTACTATTTGCTTCCAAAGGATCAGGCCCTGAGAACA
ATGACCTTATTTCCTACAACAGTGTCTGGGTTGCGTGCCAGCAGATGCCTCAGATA
CCAAGAGATAACAAAGCTGCAGCTCTTTTGATGCTGACCAAGAATGTGGATTTTGT
GAAGGATGCACATGAAGAAATGGAGCAGCTGTGGAAGAATGTGACCCTTACTCTG
GCCTCTTGAATGATACTGAGGAGAACAACTCTGACANCCACAATCATGAGGATGAT
GTGTTG

Sequence ID - 1181 SEQ ID NO: 399

nt:

155

Sequence ID 1182SEQ ID NO: 400

Sequence ID - 1183SEQ ID NO: 401

nt:

479

CGTGGCAGCCATCTCCTTCTCGGCATCATGGCCGCCCTCAGACCCCTTGTGAAGCC
CAAGATCGTCAAAAAGAGAACCAAGAAGTTCATCCGGCACCAGTCAGACCGATATG
TCAAAATTAAGCGTAACTGGCGGAAACCCAGAGGCATTGACAACAGGGTTCGTAGA
AGATTCAAGGGCCAGATCTTGATGCCCAACATTGGTTATGGAAGCAACAAAAAAAC
AAAGCACATGCTGCCCAGTGGCTTCCGGAAGTTCCTGGTCCACAACGTCAAGGAGC
TGGAAGTGCTGCTGATGTGCAACAAATCTTACTGTGCCGAGATCGCTCACAATGTT
TCCTCCAAGAACCGCAAAGCCATCGTGGAAAGAGCTGCCCAACTGGCCATCAGAGT
CACCAACCCCAATGCCAGGCTGCGCAGTGAAGAAAATGAGTAGGCAGCTCATGTGC
ACGTTTTCTGTTTAAATAAATGTAAAAACTG

Sequence ID - 1185 SEQ ID NO: 402

nt:

628

Sequence ID - 1186SEQ ID NO: 403

nt:

494

CCAACGAGGTGGCCGAATCTTCCTTCAGGATATCAAGAAACCAGACTGTGATGAC TGGGAGAGCGGGCTGAATGCAATGGAGTGTGCATTACATTTGGAAAAAATGTGAA TCAGTCACTACTGGAACTGCACAAACTGGCCACTGACAAAAATGAC

Sequence ID - 1188SEQ ID NO: 404

nt:

599

GGGAGACAAGCCCAGCCTTTCGGCGAGNATACGTCTAACCCTGTGCAACAGCCACT
ACATTACTTCAAACTGAGATCCTTCCTTTTTGAGGGAGCAAGTCCTTCCCTTTCATT
TTTTCCAGTCTTCCTCCCTGTGTATTCATTCTCATGATTATTATTTTAGTGGGGGC
GGGGTGGGAAAGATTACTTTTTCTTTATGTGTTTGACGGGAAACAAAACTAGGTAA
AATCTACAGTACACCACAAGGGTCACAATACTGTTGTGCGCACATCGCGGTAGGGC
GTGGAAAGGGGCAGCCANAGCTACCCGCAGAGTTCTCAGAATCATGCTGAGAGAG
CTGGAGGCACCCATGCCATCTCAACCTCTTCCCCGCCCGTTTTACAAAGGGGGAGG
CTAAAGCCCAGAGACAGCTTGATCAAAGGCACACAGCAAGTCAGGGTTGGAGCAGT
AGCTGGAGGGACCTTGTCTCCCAGCTCAGGGCTCTTTCCTCCACACCATTCAGGTC
TTTCTTTCCGAGGCCCCTGTCTCAGGGTGAGGTGCTTGAGTCTCCAACGGCAAGGG
AACAAGTACTTCTTGATACCTGGGATACTGTGCCCAGAG

Sequence ID 1189SEQ ID NO: 405

GGGAGACAAGCCCAGCCTTTCGGCGAGATACGTCTAACCCTGTGCAACAGCCACTA
CATTACTTCAAACTGAGATCCTTCCTTTTGAGGGAGCAAGTCCTTCCCTTTCATTT
TTTCCAGTCTTCCTCCCTGTGTATTCATTCTCATGATTATTATTTTTAGTGGGGGCG
GGGTGGGAAAGATTACTTTTTCTTTATGTGTTTTGACGGGAAACAAAACTAGGTAAA
ATCTACAGTACACCACAAGGGTCACAATACTGTTGTGCGCACATCGCGGTAGGGCG
TGGAAAGGGGCAGGCCAGAGCTACCCGCAGAGTTCTCAGAATCATGCTGAGAGAGC
TGGAGGCACCCATGCCATCTCAACCTCTTCCCCGCCCGTTTTACAAAGGGGGAGGC
TAAAGCCCAGAGACAGCTTGATCAAAGGCACACAGCAAGTCAGGGTTGGAGCAGTA
GCTGGAGGGACCTTGTCTCCCAGCTCAGGGTCTTCCCCACACCATTCAGGTCT
TTCTTTCCGAGGCCCCTGTCTCAGGGTGAGGTGCTTGAGTCTCCAACGGCAAGGGA
ACAAGTACTTCTTGATACCTGGGATACTGTGCCCAGAGCCTCGAGGAGT

Sequence ID 1190SEQ ID NO: 406

Sequence ID 1191SEQ ID NO: 407

Sequence ID 1192SEQ ID NO: 408

GTCTGGAACTCCAGACCTCAGGTGATACCCCTGCCTCAGCCTCCCAATGTGCTGGG
ATTACAGCTGTGAAGCCACCGCGCCCGGCTGCTGTGATAGTTGAGATGTAAACCAA
AAATAAAATTCTAAGCCACCCAATCCGACTGAATGGACCCTTCCTGTTGAGCAAGG
ACATTCCAAAGTAAACTGAAAAGACCAGCTTAGGCCATGATGGGAAGGGGAGGTGT
CAACATGCCTCATTCTACCTTCCTCCCTCTGGAATCCAGACAAACTGACCAGCAT
TAACATTAAAACAGAGATCTTAAGCTGGGCACGGTGGCTCATGCCTGTAATCCCAG
CACTTTGGGAGGCCAAGGTGGGATCACCTGAGACTCAAGACCAGCCTGG
CCGGTATGGTGAAGCCATGTCTCTACTGAAAATGCAAAATTGGCCGGACATTGTGG
TGCA

Sequence ID 1193SEQ ID NO: 409

TNCNTTTTTTTCCCNCGGGAAAGCGCGCCATTGTGTTGGTCCCCGGGAATTCGCG

GCCGCGTCGACGAGAAATGGCTTGAACCCAGTAGGCAGAGGTTGTAGTGAGCCCAG AATNGGNCACCTGCACNTTTANCCNTGGGTGACAAAANTGAAAACTTTGTCTNAAA AAAAAAAAAAAATTTTAANTNAAATNAAAANCCTTTNCNTTNTTTTTNAAAN GGGGCCNANNCCCCNTTTTANAAAANCCNGNTTTTNAAAAAANTTTTTTNCCCNCN NTTNGGGGGGGGGTTTTNANCNNTNTTNGGGGGGGNNCCCCTNTTANNACCNNC AAANTTTTTANTTTTTTGNNNAANNNCCCCCTTTTTTNNTTTTTTTTTGNGGGGGGG GGGNNGCCCCCNNCCTTTNGGGGGGGGGGTTTNNGNAAAANNACTTTTNAAAANNA AGGGNNGGGGGNANATNNCCCCCCCNGGNTTTTTTTTTAAAAANTNAANNGGGGG GGGNNNCTNANTNGGGGCNCCCANNGGGGGNTTANAANNATTTTCTNCCCAAACCC CCNGNTTTTATNNCCCCCCCCCCCCCNNNNGAANGGGNGGNCCNTTTTTTTATT TTTTNGGNAAANCCNNGGGGGGNTCCTTTTTNAAANNNNCCCCCAAAAAAAANTTT TTTTNTTNTTTTTCTCTNGGGGNCCNNANTTNTANANTTTTNCNCCNAAAAAAA ANGGGNCCCCTTTTTTTNCNGGNNGGNNCCCAAAANNTTTTTTTTTNAAAAAAAAA AAAA

Sequence ID 1195SEQ ID NO: 410

GTTCGTGACNTTCGGAGCTACCTGACAGAGCAGAGTCAACCAGGNTCTGCCCAAAG
AGAGTGTTAGGCCTGAGCTTGAGAGCCCTGGAGAGACGTGTGCACAAAATGTGACC
TGAGGCCCTAGTCTAGCAAGAGGACATAGCACCCTCATCTGGGAATAGGGAAGGCA
CCTTGCAGAAAATATGAGCAATTTGATATTAACTAACATCTTCAATGTGCCATAGA
CCTTCCCACAAAGACTGTCCAATAATAAGAGATGCTTATCTATTTTA

Sequence ID - 1196SEQ ID NO: 411

nt:

412

CCGCCAACATGGGCCGCGTTCGCACCAAAACCGTGAAGAAGGCGGCCCGGGTCATC
ATAGAAAAGTACTACACGCGCCTGGGCAACGACTTCCACACGAACAAGCGCGTGTG
CGAGGAGATCGCCATTATCCCCAGCAAAAAAGCTCCGCAACAAGATAGCAGGTTATG
TCACGCATCTGATGAAGCGAATTCAGAGAGGCCCAGTAAGAGGTATCTCCATCAAG
CTGCAGGAGGAGGAGAGAAAAGGAGAGACAATTATGTTCCTGAGGTCTCAGCCTT
GGATCAGGAGATTATTGAAGTAGATCCTGACACTAAGGAAATGCTGAAGCTTTTGG
ACTTCGGCAGTCTGTCCAACCTTCAGGTCACTCAGCCTACAGTTGGGATGAATTTC
AAAACGCCTCGGGGACCTGTTTGAATTTTTTCTGTAGTGCTGTATTATTTTCAATA
AATCTGGGACAA

Sequence ID 1198SEQ ID NO: 413

CAGAGGTGGGAGGATTGCTTCAGTTCAAGAGTTTGAGACCAGCCTGGGTAACATGG
CGAAACCCTGTCTTTACAAAAAATGCAAACCTTTGCCGCATGTGTTGGGGTGCGCC
TGTAGTCCCAGCTTCTCGGGAGGCTGAGGTGGGGGGACCACCTGAGCCATGGAGGT
TGAGGCTGCAGTGAGCCGTGATACCACCACTGTACTCTAGCCTGGGCCATAGAGTG
AGACACCCTGCCTCAGAAATA

Sequence ID - 1199SEQ ID NO: 414

nt:

439

Sequence ID - 1200SEQ ID NO: 415

nt:

526

GACCCCTGGACCTGGGGCCCAGTCGGCCCTCANAGCCCTTGCCCGCTCGGGTATGA
AGATCGGGCGGATTGAGGATGTCACCCCCATCCCCTCTGACAGCACTCGCAGGAAG
GGGGGTCGCCGTGGTCGCCGTCTGTGAACAAGATTCCTCAAAATATTTTCTGTTAA
TAAATTGCCTTCATGTAAACTG

Sequence ID - 1201 SEQ ID NO: 416

nt:

613

Sequence ID 1202SEQ ID NO: 417

Sequence ID - 1203SEQ ID NO: 418

nt:

692

TGCAGAGGGGTCCATACGGCGTTGTTCTGGATTCCCGTCGTAACTTAAAGGGAAAC

TTTCACAATGTCCGGAGCCCTTGATGTCCTGCAAATGAAGGAGGAGGATGTCCTTA
AGTTCCTTGCAGCAGGAACCCACTTAGGTGGCACCAATCTTGACTTCCAGATGGAA
CAGTACATCTATAAAAGGAAAAGTGATGGCATCTATATCATAAATCTCAAGAGGAC
CTGGGAGAAGCTTCTGCTGGCAGCTCGTGCAATTGTTGCCATTGAAAACCCTGCTG
ATGTCAGTGTTATATCCTCCAGGAATACTGGCCAGAGGGCTGTGCTGAAGTTTGCT
GCTGCCACTGGAGCCACTCCAATTGCTGGCCGCTTCACTCCTGGAACCTTCACTAA
CCAGATCCAGGCAGCCTTCCGGGAGCCACGGCTTCTTGTGGTTACTGACCCCAGGG
CTGACCACCAGCCTCTCACGGAGGCATCTTATGTTAACCTACCATTGCGCTG
TGTAACACAGATTCTCCTCTGCGCTATGTGGACATTGCCATCCCATGCAACAACAA
GGGAGCTCACTCAGTGGGTTTAATGTGGTGGATGCTGGCTCGGGAAGTTCTGCGCA
TGCGTGGCACCATTTCCCGTGAACACCCATGGGAGGTCATGCCTGATCTTTC
TACAGAGATCCTGAAGAGAT

Sequence ID 1204SEQ ID NO: 419

Sequence ID 1205SEQ ID NO: 420

TNNNNTNNCNNCNANTAANNCANNTCNANNNNANNNAATTACTTNNANGTNNNTC ACN

Sequence ID - 1207SEQ ID NO: 421

nt:

642

ACGAGAAGCCAGATACTAAAGAGAAGAANCCCGAAGCCAAGAAGGTTGATGCTGGT GGCAAGGTGAAAAAGGGTAACCTCAAAGCTAAAAAGCCCAAGAAGGGGAAGCCCCA TTGCAGCCGCAACCCTGTCCTTGTCAGAGGAATTGGCAGGTATTCCCGATCTGCCA

Sequence ID 1208SEQ ID NO: 422

CCCTATACCTTCTGCATAATGAATTANCTAGAAATAACTTTGCAAGGGAGAGCCAA
AGCTAAGACCCCCGAAACCAGACGAGCTACCTAAGAACAGCTAAAAGAGCACACCC
GTCTATGTAGCAAAATAGTGGGAAGATTTATAGGTAGAGGCGACAAACCTACCGAG
CCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTAGTTCAACTTTAAATTTGCCCA
CAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAGTCCAAAGAGGAACAGCTC
TTTGGACACTAGGAAAAAACCTTGTAGAGAGAGGTAAAAAATTTAACACCCATAGTA
GGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACCCACTACCTAA
AAAATCCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCC
TATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAG

Sequence ID - 1209SEQ ID NO: 423

nt:

620

CTCTCCTGTCAACAGCGGCCAGCCTCCCAACTACGAGAATGCTCAAGGAGAGCAG
GAAGTGGCTATGCTGGGGGGCGCCCCACAACCCTGCTCCCCGACGTCCACCGTGAT
CCACATCCGCAGCGAGACCTCCGTGCCCGACCATGTCGTCTGGTCCCTGTTCAACA
CCCTCTTCATGAACACCTGCTGCCTGGGCTTCATAGCATTCGCCTACTCCGTGAAG
TCTAGGGACAGGAAGATGGTTGGCGACGTGACCGGGGCCCAGGCCTATGCCTCCAC
CGCCAAGTGCCTGAACATCTGGGCCCTGATTTTTGGGCATCTTCATGACCATTCTGC
TCGTCATCATCCCAGTGTTGGTCGTCCAGGCCCAGCGATAGATCAGGAGGCATCAT
TGAGGCCAGGAGCTCTGCCCGTGACCTGTATCCCACGTACTCTATCTTCCATTCCT
CGCCCTGCCCCCAGAGGCCAGGAGCTCTGCCCTTGACCTGTATTCCACTTCCA
CCTTCCATTCCTCGCCCTGTCCCCACAGCCGAGTCCTGCATCAGCCCTTTATCCTC
ACACGCTTTTCTACAATGGCATTCAATAAAGTGTATATGTTTCTGGTGCTGCTGTG
ACTT

Sequence ID 1210SEQ ID NO: 424

Sequence ID 1211SEQ ID NO: 425

Sequence ID - 1212SEQ ID NO: 426

nt:

374

AGAGCAGCAGCCATGGCCCTACGCTACCCTATGGCCGTGGGCCTCAACAAGGGCCA CAAAGTGACCAAGAACGTGAGCAAGCCCAGGCACAGCCGACGCCGCGGGCGTCTGA CCAAACACACCAAGTTCGTGCGGGACATGATTCGGGAGGTGTGTGGCTTTGCCCCG TACGAGCGGCGCGCCATGGAGTTACTGAAGGTCTCCAAGGACAAACGGGCCCTCAA

Sequence ID - 1213SEQ ID NO: 427

nt:

567

Sequence ID - 1214SEQ ID NO: 428

nt:

620

CTCTCCTGTCAACAGCGGCCAGCCTCCCAACTACGAGAATGCTCAAGGAGAGCAG
GAAGTGGCTATGCTGGGGGCGCCCCACAACCCTGCTCCCCGACGTCCACCGTGAT
CCACATCCGCAGCGAGACCTCCGTGCCCGACCATGTCGTCTGGTCCCTGTTCAACA
CCCTCTTCATGAACACCTGCTGCCTGGGCTTCATAGCATTCGCCTACTCCGTGAAG
TCTAGGGACAGGAAGATGGTTGGCGACGTGACCGGGGCCCAGGCCTATGCCTCCAC
CGCCAAGTGCCTGAACATCTGGGCCCTGATTTTTGGGCATCTTCATGACCATTCTGC
TCGTCATCATCCCAGTGTTGGTCGTCCAGGCCCAGCGATAGATCAGGAGGCATCAT
TGAGGCCAGGAGCTCTGCCCGTGACCTGTATCCCACGTACTCTATCTTCCT
CGCCCTGCCCCCAGAGGCCAGGAGCTCTGCCCTTGACCTGTATTCCACTTACTCCA
CCTTCCATTCCTCGCCCTGTCCCCACAGCCGAGTCCTGCATCAGCCCTTTATCCTC
ACACGCTTTTCTACAATGGCATTCAATAAAGTGTATATGTTTCTGGTGCTGCTGTG
ACTT

Sequence ID 1215 SEQ ID NO: 429

AGTCCAAGTAAATGATCACTTTATTTGCTAGGGAGGGAAGTCCTAGGGTGGTTTCA
GTTTCTCCCAGACATACCTAAATTTTTACATCAATCCTTTTAAAGAAAATCTGTAT
TTCAAAGAATCTTTCTCTGCAGTAAATCTCGCAGGGGAATTTGCACTATTACACTT
GAAAGTTGTTATTGTTAACCTTTTCGGCAGCTTTTAATAGGAAAGTTAAACGTTTT
AAACATGGTAGTACTGGAAATTTTACAAGACTTTTACCTAGCACTTAAATATGTAT
AAATGTACATAAAGACAAACTAGTAAGCATGACCTGGGGAAATCGCCATGGCAACAGGC
TTTAAAAAAAGACCCTTGAAAAGTAGCAAGTGACCAGAATCTGCCATGGCAACAGGC
CTCTCTGTACATTTGCTAGCTTGTAGTTTTCTAAGACTGAGTAAACTTCTTATTTT
TAGAAAGTGGAGGTCTGGTTTGTAACTTTCCTTGTACTTAATTGGGTAAAAAGT

Sequence ID - 1216SEQ ID NO: 430

nt:

484

Sequence ID 1217SEQ ID NO: 431

Sequence ID 1218SEQ ID NO: 432

CTCACTTGGTGGGTGAGCCTCCAATGACTACACCCAAGGAGGATTTAACACAGGGA
TTTTATGACTTGCAACAAGTCAGGAGGACATGGGGTTGGGGTAGTTCAGCAGTGCC
TGTCTGAACAAAGGTGAAAATTGGGCTTTTATTGGGCTGATCAAGGGGGAGTAAAG
GCAGCCAGGAGCAGTCGCCTGTCATGCTTCTACCTATATTGCATGTATAGAAAAGG
GAAAATAAACTCCTTCCTGGGCAGGGTTTTAGTATGCTAAGGAGGGGAGTTATTCA
ACTTCAATCCAACTCAAGCATCAGCATTGCTGCGTCCATCCCAGTTTTGTTTTGCT
GGGGCTGAACTTCTTCCTATAACTTTTTGAAACAACAAGAACTCAAGGTGTGACAG
TTACAAGTGGGCCCTTTTTCACAGTGTGTACCTAAACACGTGAGGACCCTGGATTA
CAGAATGACAGACTCGAAGTGACTCAAGTTCCGGTTGTTCATCTTTAGATGGTAAA
GATGGCTGTACGTACTATCCTTGCTTATTTCCAATCTATTGTTTAAACTCTTGTAT
ATGTAATACCGCAGAGGCTAGAGATACAACATGGTGTGAATGAGTGAATTCAAGT
AATCCATTACTAATGTGATCTGGAAACAACATGGTGTTGAATGTGCATATGT

Sequence ID - 1219SEQ ID NO: 433

nt:

559

Sequence ID 1220SEQ ID NO: 434

GANNNGTGCGATANNATGNNTGTCTTTTTTTTAAAGTNTTTCNNATNGNAGNGAAN
CCCCCNNANNTNNCATAANGAGAGATNACTACNGTACANATAGNGNCANACNGATA
GTAGTANCAANATTGTNTTAGCTANATNANTCAATAGATATCNAGATANAANAANA
NCNNGGATATACAGCGATGTNTNANNGGNNNNNNNANGGAACGAACATCNACNTTA
ANNATAAGCTNGNGGAGAGAGACANGTANGTTATANANNAGAATNGNAGTAGGNGT
GATCATAATAGNNNNNANNTANTATATANGATNTTANTGNNCTNTNNTNNGTTTAT
CNNNAATNTCTATNCTNGAGAGNAGCNNNATNNNNAGGCGANGANATTGGGNNNTN
CTCNTNATAGANANCTGGTGTCNNANAANTACNTCATCTATTNANCTCTCACNANA

TGGNANNATANAGNAGNGNNNTNNANAGGANTANGCATAGNGNNTNNCTNAAACAA AANNNATAAGANNTCTCGNNAANANGGGCCTNTNNTNTAGCGAGGNNTTANTTTNT ATANTTNTTCNCTCTTNNAATANNTANGATANATGANCTNGNNGTGATANATANNN NNTACNGTNAANNTNTANTCNTATAATAGATANAAATATAGGATNTTNCTCTGGCN GGTNGAANANTTNNTNCNNTTTNAATAATGNTGTTAGNGACNGNGNTNTNANANNN NNTTAGAAAGGTACTCTATATACTNNTATGNTNCGGCNNATAATANAACAGATGTT TGTATNAATATNAAANAAGGTCNNTTTCGNCAAGAGAANNNTGNCTGGTNATAGAA TTAGCATAANTTANNTANTATGATNNANTNNTNCTACNANTNTTAGCNNTTNGCAG NAGTCATTNNGNATNTATNNNGNNTANTAGTNANTTGGGNCTNNTNCAGANTATAT TNTGNGAANATGAANNTACGNANTCCTNNGNANTATNATNNTGANTANGANAANCN ANANNTNTTNTANNANTGNCTATANATTGCCNNGATANATTNTNNNAATGAANCGA TAGCCCGCNCTAAGGANNTNNGTNANNTAAANNTCTCAGATAANNTACNTNTTNNT TATTAANCNANNATCACANTATANCNGNGACANNNGCGANANTATATGTATGNNAN TATNACNGNTCCNNNCCGNGAANNTANTCNTANNAGGCATTCNGNNGAGCTNTTCT NCTAGACNATTTNNANTGAAANNATGCNGNNAAAAACGACNNNCTTNAANTTNTGT CTACANTCCGCNNTNTTTNTACAGATNGCAGNTAAGNNNANTNANNGCTCTCANCT NGCTNNNACT

Sequence ID - 1221 SEQ ID NO: 435

nt:

741

485

Sequence ID 1226SEQ ID NO: 437

Sequence ID 1228SEO ID NO: 438

741

Sequence ID - 1231 SEQ ID NO: 440

nt:

203

TTGAGGAAGGGTCTACTGTCTTTTTAAATGGCACAATTTTAAGAGGTTTGAGAGGT
ACAGTCCCTTAACCTGCCACGGGAGAGGGGCCCCCAAACTTTCTTCCCCCCACACT
TCTGGTTTTCTGTGTGGAGGGGGGAGCAGGGATATCTAAGCTGTGGTGAAAGGGT
AGGAGAGATGCTGGAGGTGGGGGTGCTGTTCTA

Sequence ID 1239SEQ ID NO: 441

Sequence ID 1255SEQ ID NO: 442

TCACTTCGTATNGAANCTGTTTGGACTTGCTCAACAAGACCTTATCTTAACAAAAA GTAACTTATAGAAAAGGGAGACATTCATTTAACTTCAAGCCCATATTATTCTTAAA AGCTGACTCTTGAAATAGTATTTATTGAGTCATAGTGGAGTCATGGGACTTTTTAA GGGCCGGAAGGGACTATTTAGATCATCCAGTCCCACCCTGTCATTTTATGGAGGAG GAAACTGAGGCCTAGATAAGATAACCAGTTAGTGGGTCCACTGACCTTTAGGACAG TAGTCTATCCGTAAGAGACAACATGGAGAAAGAAATACAACGTTTTTATAGTGAAT TATCATCTTACAAAGAATATTCTTCCCATATCGCACTTTTAAAAAAGTGGGTACCTT AGTCAAATAGGAGAAAAAACCACTTGAGTAGTTTCATCCTCAGGTTTTAGGTGAGG AAACTGATACTCAGATTAAATAACTTTAAGCACACAGAGCCTGAATGATAGTCTTA TTTGAGCTCATCTGTGCTTTTAATGTGTACTACGTTAGGTGTTTTCACTTGCATTT CCTTTAGTCTTATTTGAGCTCATCTGTGCTTTTAATGTGTACTACGTTAGGTGTTT TCACTTGCATTTCCTTGTTTGACGTTGACAATAAATCGTGAAGCTGCCTTATCTAA GNAGTCCTAAAGTAAATCATTGGAACACATGTANCCAGTTTGTTGTTTTTATTTGC CAGGTNTCAAATATAACTGAAAACCCATGCTAACTGACTNATTTTAAAAGNTGTNT GGGGCATGAAANGATTGCTCTGCCTGGGCGGGNGGTTNANCCTGNGTCCCCCNTTT NGGAGNCCACCCANGANGCGATATTTNAGGGNNGATTCNAAACCCCTGGCACGNGN NAACCCCNTTTTTAAANANAAAANANCGGNNG

Sequence 1256SEQ ID NO: 443

TCATTTCAAGAAGTCCCCTCTCCTCCACATTTGTTTTTGCCAATTTGCACATTAAAT
GACTCTTCCCTCAAATGTGTACTATGGGGTAAAAGGGGTAGGGNTTAAANATGTAA
ACAGTTGGGTTTTTTAAGGGNCCTTTTTCATAACTGGAACACTCTNTACAAGGNTN
CTTNTTAAATAAATAACTTGACTTTTTTTTTTTTTTAAANGNANCTTCNTGCTTCCA
TAAAAAAAAAAATTTAANTNGNCANCTNTGCTGCGCGNCCANTTNGCTNGNCCNT
GGCATTCCCTAGGGANGNTNAATANTGGCNNNTTAACNNGGCNGNAACNNNNNCCA
NT

Sequence ID 1331SEQ ID NO: 444

Sequence ID 1332SEO ID NO: 445

TAAAAAATAAAGAAAGGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTG GGAGGCCGAGGCGGTGGATCATGAGGTCAGGAGATCGAGACCATCCTGGCTACCA NGGTGAAACCCCCGTCT

Sequence ID 1335SEQ ID NO: 446

Sequence ID 1336SEQ ID NO: 447

Sequence ID 1337SEQ ID NO: 448

CAAGAACTCTGGGACATTTGCAAAGGGTATGGCATATGTGTAATGGGAATACCAGA

Sequence ID 1338SEQ ID NO: 449

Sequence ID 1344SEQ ID NO: 450

AAGCAAGAGGAAATTGGCTGGGCACAGTGGCTCTGTAATCCCAGCACTTTGGGAGG
CTGAGGTGGGTGGATCATGAGGTCAAGAGATTGAGACCATCCTAGCCAACATGGTG
AAACCCCATCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGTGGCACACGCCTG
TAATCCCAGCTAGTCAGGAGGCTGAGGCAGGAGAATATCTTGAACTTGGGAGGCAG
AGGTTGCAGTGAGCCAAGATTACATCACTGCACTCCAGCCTGGTGACAGAGCGAGA
CTCCGACT

Sequence ID 1348SEQ ID NO: 451

CTGAAACTGCACTGAACCCACAGGTAGGTTACATCACAGGACAGAAATCTGAGGAG CTGGAGAAAGCAAAAGAATAAAGGATGGGCTGACACCAGAAGGAATTAAAGGAATT TTTGCTGTTACTTAAATATAGTGTTTTGAAAGTGTTTCAAATGTATTCAAGTTGGG ATTTTCCATATTTTACTACAGTTCTGTCTTAGTATGTTCACCATAAAACACTTATC ATTAAAGCTCACAAAGTGCTTTTTTGTAATATGAGGATAAAATGAAGCCATATAAG AATTTTTTTATATCTGTACATTTAACCCACATTTGAGCCTTTAGCCAAAATATATAG CTTTTTTTTTTCTGACCTGGCCAACGTATTATCCAGCAAACATCAACTGAAGCAAT ATGGAAACACTTCCAAATGTTTGCCAATAATGCTATTAAGTGACTGATGTCAACAT TAGTTACATGGCAAACTAAAGAGGCATTATACATTTTTAAAACACACTAACATATA ACTGTAGATAATGTAAGGTTTATTTATATGCATATTTCATAGTATATTTAAATGTT TGATATCTCTTTCCAGGCTACTAATAAAATTGCCAGAACTAAACTATCAGGTAAAG GTTAAGGCATCAATTGACAAGTAAGTTTTCTAATTTCGTTTTGAATTACAATTCCA AATGTAAGACTTTTAAAAATGAATGGCCTTTATTTTATAGAATAATTTTGACCTTT TAAATTTACTTATCTAACATTATATAATGAATGTACTTCAAATATTTGACTTTGAA GTCAACATTAACAAATTCATGGATCCTAATTAAAATTTACTATAAAACTGGAATCA TTTATTACTTCCTT

Sequence ID 1351SEQ ID NO: 452

TTTTTTTTTTTTAAAAGAGATGGGTTCTCACTATGTTGCCCATAATGTTTATGAG
ATTAAGTTCATCTTTTTTATCTGAGTAGTATTTTATTGTATGAATATACCACCATT
TATTTATCTGTTGGTTATTTCCAGTTTTTGGGCTATAATCCAAAATGCTTTTTTCAA
ACAATAGGCTATATATCATTAATGTCCGTTTATCAGCAGTATAAAATATCTTACCA
TAAATATTAATAAAAGAAGCATTCATATATAAAATATAGATATTTCAAACCCTACA
GAGGGCCTTTTAATGATTAAATATTTTGTCCTTACAAAAAGGTCCAGGTAATTACA
CCCATGAGGTTAACCTGCCTTAGTGCAGGACTTAAAATAAGGCTTCTCCTGCCATC
TCTCTCCATTTGTAGAATGTGAAATTCTTTAAAATGCATCCTATATTAGGAATACT

ATAGCTGTGCACTGGTGTTTGTTCTCTTCTTTAAACTCGGGACCGTATATATCTGC
TCAAATTGCCCAAGTATACATATGCTGCACTCCATCAAGTGTCAGGCCACATTCTA
TCAGCACAGCGTGACTGCCTATCAGTGACAATATAAGTGAGCTCTATTTGGATCCC
TCTTACCCTACCTTTTATATTTATGACAGCATTATCATAAAACTCCAATATTCTTC
AATAACTTACATGTTTGTTGTTGTAGGATAAAATTATTACCCTCAATGAACTACAT

Sequence ID 1352SEQ ID NO: 453

Sequence ID 1353SEQ ID NO: 454

Sequence ID 1355SEQ ID NO: 455

TGGTCTTTCACCCAGCCAGGGAGAAGGTTCTTCGCTCAGTATGAAGAAAAGCAACC

Sequence ID 1359SEQ ID NO: 456

CGGGATCCCTAGTATAACACATTCAGTGTTCCCCTTTCAGTCTTACTACTTTGACC
GCGATGATGTGGCTTTGAAGAACTTTGCCAAATACTTTCTTCACCAATCTCATGAG
GAGAGGGAACATGCTGAGAAACTGATGAAGCTGCAGAACCAACGAGGTGGCCGAAT
CTTCCTTCAGGATATCAAGAAACCAGACTGTGATGACTGGGAGAGCGGGCTGAATG
CAATGGAGTGTGCATTACATTTGGAAAAAATGTGAATCAGTCACTACTGGAACTGC
ACAAACTGGCCACTGACAAAAAATGACCCCCATGTGAGTATTGGAACCCCAGGAAAT
AAATGGAGGAAATCATTTGCCTTAGGGATTGGGAAAGCTGCCCACTAACTGTCTTC
CCCATTGTTTTGCAGTTGTGTGACTTCATTGAGACACATTACCTGAATGAGCAGGT
GAAAGCCATCAAAGAATTGGGTGACCACGTGACCAACTTGCGCAAGATGGGAGCGC
CCGAATCTGGCTTGGCGGAATATCTCTTTGACAAGCACCCCTGGGAGACAGTGAT
AATGAAAGCTAAGCCTCGGGCTAATTTCCCCATAGCCGTGGGGTGACTTCCCTTGGT
CACCAAGGCAGTGCATGCATGTTGGGGTTTCCTTTACCTTTTCTATAAGTTGTACC
AAAACATCCACTTAAGTTCTTTGATTTGTACCATTCCTTCAAATAAAGAAATTTGG
TACC

Sequence ID 1360 SEO ID NO: 457

Sequence ID 1361SEQ ID NO: 458

Sequence ID 1364SEQ ID NO: 459

Sequence ID 1365SEQ ID NO: 460

CACCAGGCTGTCTTCAGATACTTCATACAGAAATGAGCCTCCCTGTGGGGTCCTCT
TCCCTCCTTCAGCCTGTCCATCAACACAGCATTGCGGGATCCTTACCATGGCATCC
AGCCCTGGAGATGCTTCAGGAAAGTTGCAGGTCCATGCTGCAGGACAGGCTCAGAT
CAGCAGAGACGCATCTCACATCGGGCTGTGAAATTCAAGTTGAGCTGCAATTGGCA
ATGAGAA

Sequence ID 1366SEQ ID NO: 461

Sequence ID 1367SEQ ID NO: 462

TTCGTGAGTGATGGCGTCCCGGGTTGCTTGCCGGTGCTGGCCGCCGCCGGGAGAGC CGTTCCTGACCCGGCCTAAGGTCCCTGTCTTGCAGCTGGATAGCGGCAACTACCTC CTGCTGCCCTGTACTATTTAGTGGTCCAAGGCAAGAAGGGGGAAGATGTTCTTGGT TCAGTGCGGAGAGCCCTGACTCACATTGACCACAGCTTGAGTCGTCAGAACTGTCC TTTCCTGGCTGGGGAGACAGAATCTCTAGCCGACATTGTTTTGTGGGGAGCCCTAT ACCCATTACTGCAAGATCCCGCCTACCTCCCTGAGGAGCTGAGTGCCCTGCACAGC TGGTTCCAGACACTGAGTACCCAGGAACCATGTCAGCGAGCTGCAGAGACTGTACT GAAACAGCAAGGTGTCCTGGCTCTCCGGCCTTACCTCCAAAAGCAGCCCCAGCCCA GCCCGCTGAGGGAAGGGCTGTCACCAATGAGCCTGAGGAGGAGGAGCTGGCTACC CTATCTGAGGAGGAGATTGCTATGGCTGTTACTGCTTGGGAGAANGGCCTAGAAAG TTTTGCCCCCGCTGCGGCCCCAGCANAATCCAGTGTTGCCTGTGGCTGGAGAAAGG AATGTGCTCATCACCAGTGCCCTCCNTTACGTCAACAATGTCCCCCACCTTGGGAA CATCATTGGTTGTGTGCTCAGTGCCCGATGTCTT

Sequence ID 1368SEQ ID NO: 463

Sequence ID 1369SEQ ID NO: 464

Sequence ID 1370SEQ ID NO: 465

Sequence ID 1371 SEQ ID NO: 466

Sequence ID 1372SEQ ID NO: 467

Sequence ID 1374SEQ ID NO: 468

Sequence ID 1378 SEQ ID NO: 469

Sequence ID 1380 SEQ ID NO: 470

AAAAGAACCTCACAGTTCAGCAGGGTTCTAGCATGAGACAATGAGGACAAGGGTAG
GTGAGCAGGTGGAAAGAGTGAGAACAGGTCAATTGTGATGAGAAAAATAATAAAGA
CAGAAAAGGCAGAAGACTGCCTGGCAGAAGACCTGTCCCAGCAGATACAAAAATAC
AGACAACAGGAGCCAGCATAGACCCTTGACCTGTGTAAGTCTTTCTCAGGCCTTCT
TTTAAGTAGAAACATGCCTTTGAAAAAAAAGTTTTAATAAACAGGAAAAATCATAAAT
CCCTATTTACATAAATAATATATCCTGGTCTTATTCTTAAAACCATTGATTTTTCA
CGGCTCATTAANAAAGCTGGGCGAGGTGGCTCACGCCCGTCATCCTAGCACTTTGG
GAGGCCGAGGCGGCANATCACAAGGTGAGGAGTTGGGAGACCAGCCTGACCAACA
CGGTGAAACCCAGTCTCTACTAAAAATACAAAAATTANCTGGGGGTGGTGTGT
GCCTGTAATCCAAGCTACTCGGGAGGCTGAGGCAGA

Sequence ID 1382SEQ ID NO: 471

CTTACTACCTCCAACATGAAACAAGCAGCCCCGCACTTCTCGAAGGTCTGAGTTAC TTGGAATCGTTTTACCACATGATGGACAGAAGGAATATTTCAGATATCTCTGAAAA CCTCAAGCGTTACCTTCTTCAGTATTTTAAGCCAGTGATTGACAGGCAAAGCTGGA GTGACAAGGGCTCAGTCTGGGACAGGATGCTCCGCTCGGCTCTCTTGAAGCTGGCC TGTGACCTGAACCATGCTCCTTGCATCCAGAAAGCTGCTGAACTCTTCTCCCAGTG GATGGAATCCAGTGGAAAATTAAATATACCAACAGATGTTTTAAAGATTGTGTATT CTGTGGGTGCTCAGACAACAGCAGGATGGAATTACCTTTTAGAGCAATATGAACTG CACAGAACTTGGCAGCTCTCCTTCATGCGATTGCCAGACGTCCAAAGGGGCAGCAA CTAGCATGGGATTTTGTAAGAGAAAATTGGACCCATCTTCTGAAAAAATTTGACTT GGGCTCATATGACATAAGGATGATCATCTCTGGCACAACAGCTCACTTTTCTTCCA AGGATAAGTTGCAAGAGGTGAAACTATTTTTTGAATCTCTTGAGGCTCAAGGATCA CATCTGGATATTTTTCAAACTGTTCTGGAAACGATAACCAAAAATATAAAATGGCT GGAGAAGAATCTTCCGACTCTGAGGACTTGGCTAATGGTTAATACTTAAATGGTCA ATAGAAAAGTAGGCTGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGA

Sequence ID 1387SEQ ID NO: 472

Sequence ID 1389SEQ ID NO: 473

GNTTTTCGGAAACGGAGTCTCGCTTTCTCGCCCACTCTGGAGTGGNGCAGTGGGGN
GGTCTCAGCTCACCACAGCCTCCACCTCCTGGGCCCAAGCGATCCTNTCACCTCAG
CCTCCTGCGTAGCTGGGACTACAGGCGTGCACCACCATTCCCAGGTAATTTTTGTA
TTTTTTGTANANACAGGGTTTCACTGTTGTTGCCCAGGCTGGTCTCGAACTCCTGC
TTCAGTCTGCCANAATGCTGGATTCTAGGCGTGAGCCACCGNGCCTGGCCCAAAAG
TTACTTTTCTTACAGAAGCAAAGCTTTAATGCATTTTACTGAATGCTTATAGCTTT
GTAGATACTGAAAAGAGTATGAGCGTCACATACAGACACATNTAACAGCACTGCCT
CCAACCAGCCCCTACCCACTGGTCAGGNGAGTAANAATCAAAATTCTTTTCTGNGA
GTGGAACGGAAATTTCATCTCTCCTCCTCAGGCAAGTAGTTAANAGGCTGGNGGGA
GTCATGGCCCCATTTTGTTCAAAATACAAGCTCCACAGGAACAAAAGGCTGAACTG
CTCACCTCCCAACTGATGAACCTCGTCTTTGTTCCATGTCAAAAGGGCCCTTTGTGT
TACTGCAGCAGAAACTCCAGCTATCAAACCATCAGGCACCAAAAGTAAAACTCCTT
TCTCTAAAAAAGACCTCTCTTTTACCTGAGCCTTTCCATGTCCAAAAGTAAAACTCCTT
TCTCTAAAAAAGACCTCCCAGAGGAANACCAGCGCTTGCCTAGTGAAATTATAC
TATGAGACAAGGGTAAAAGACCTCCAAANACCGGGTTGGCAGGTAAGGGAGTAGGGN

Sequence ID 1390SEQ ID NO: 474

Sequence ID 1391SEO ID NO: 475

Sequence ID 1392SEQ ID NO: 476

Sequence ID 1394SEQ ID NO: 477

Sequence ID 1395SEO ID NO: 478

CAACATTTGTTTAGCTTGCTTTGGCTTTAATTATCTAAAGCCAATGAAAGACTTCTT TGTTGATTTTTTAAGATAGAAAGATT

Sequence ID 1396SEQ ID NO: 479

CAAACACTATGTTATTTTATGAANAAGACTTGAACATCTATGGATTTTTGGTATTTG CAAGGGGTGAATGGGGTATTTGCAAGCAGTGAATGAGGAGGCCTGGAACCAATCTT CTGCTGATATTGAGGCACAACTGAAAAAGGTATATTACTTAAATCTCTTATTGTAT TGTAAACTGTATAAGTAATGAAATTAAAAGGCAGAAATTGTCAGACTGAATAAAAT GAAAAGACCAAACAATATGCTGCTTACAAGAAACACAATTCAAATATAAGGACACA ATTAGTTTAAAGGAAAAGAACTGGAAAAGATATACCATGATAACACAAGTCAGAAG AAAGCTGCTGTGGATATATTAATATGAGATGTAGATTTCAGAGCAGTGAATATTGC CAGGCATAAAGAAAGTTATTACATAATAATTAAGGTATCAGTTCATCAAGAAGATG TAATAACCCTAAGTATTTATACAACTAATATCAGAGCTTCAAAATACATGAAGCAA AAACCAGTGGAATTGATAGGAGAAACACACAATTACACAATTATAGTCAGAATTTT CAACATATCTTTCTCAATGGAGAAAACAACTAGACAGGAAATCATTAAGGATATAG ATGATTTAAATTATGATCAACTACCTGGACGTAATTGGCATTTATGGAACACTG CACCACCAACAGCAGAGTACATATTATTTTCAAGTACACAGAAAACAGTTACCAAT ATAGACCATTTTCTGGGTCATAAAACACATCTCAATAAATGTAAAACAATTAATGT TATATAAAGTATGTGCTCTGACCNCAAAGGAATTAGAGATCAATAAAAGAACATCT TTGAAAAATCTCACNTATTTAAAAACTAATAACTCACTTCTAAATAACTCCTGTNT CAAGAGAATNAAANGG

Sequence ID 1397SEQ ID NO: 480

AATTTCTGTTGAATGAACCAAAAGCAACTGCCAACCTCTCCATGCACCATGTTTT
CAGAGGAGAAAGCACAGTGAAGAATGCAGTGTTCTGAGGTCCTGTCACCCCTGA
GGCTGTGTGTGTCCTTTGCCAAATTAAAGAGTCTTACTGAATGCGGTGCATCCAGG
AGACAGGCCNAGGTTTGGACTGGTAAAAAAAAA

Sequence ID 1399SEQ ID NO: 481

Sequence ID 1440SEQ ID NO: 482

Sequence ID 1447SEQ ID NO: 483

Sequence ID 1448SEQ ID NO: 484

GGCCACCGGGTGCAAGGTCAGGGCTGGGGTGAGGCTGGGAAGCCCAGGGCTTGGC
CCACTGTGGCCGCCTTGTGTGTGTCACTGCTTTCCTGGGCCTGCTGTGAGCTCCCTC
TAGGACCCCAGGCCTGTCTGGTGGGTCACTGTGACCACCACCTTGCACAGCACCTG
GCGCGTGGCAGGTGCTCAAACATTACTTGTTTCGGAATGAACTTCATCTTGCTCTT
GGCTTTTTGACTAATGCTGTGGAACATCTGACTAATTAGTGACTCTTTTGGGGCCCC
CAGTTTCCCAGCTATAAAGTGGTAATATTAAGATAATAATTCGGCCGGGCGCGGTG
GCTCACGCCTGTAATCCCAGCAGCACTTTTGGGAGGCCGAGGTGGGCAGATCACGAG
GTCAGAAGATCGAGACCATCCTGGCTAACACGGTGAAACCCCATCTCTACTAAAAA
TACAAAAAATTANCCGGGCGTGGTGGCCGGGCGCCTGTAGTCCCAGCTACTCANGAG
GCTGANGCAGGAGAATGGTGTGAACCCGGGAGGCAGAGGTTGCAGTGAACCAAGAT
CGNNCCACTGCACTCCAGCCTGGGCAACAGAGCGAGACTCCATCTTAAAAAA

Sequence ID 1449SEQ ID NO: 485

AATCAGGGCCGCAGTGTTTCTGCGCCTGCCCAGAGCTGACTCCTGATTTAACCGC
TGGCGTAACCGCGGGTTGCACGCATGCGTGCTGAAAAGCCTTTCACCCTCACGTGG
TTTCTTTTTTAACCAGTCATCAAGCGAGGCTCGCGCGCAGGCCCCGCGTTGGAAAA
TGGCGGGGAAGCTGAAACCTCTGAATGTGGAGGCGCCAGAAGCTGCTGAGGAGGCT
GAAGGTAGTGAGGCAAGTGGGCTGCACTCCTTTCTCTCCAACCAGGGCAGAAAGG
AGGGAGGATTCGTCCCATTACAATAATGAAATAATGATATTCTAATTTTTTTAAAT
AAAATGTTAAGCCTTTTGTTATTGAA

Sequence ID 1450SEQ ID NO: 486

GGAAANCATGAGGCTTCGGGAGCCGCTCCTGAGCGGCAGCGCCGCGATGCCAGGCG CGTCCCTACAGCGGCCTGCCGCCTGCTCGTGGCCGTCTGCGCTCTGCACCTTGGC GTCACCCTCGTTTACTACCTGGCTGGCCGCGACCTGAGCCGCCTGCCCCAACTGGT CGGAGTCTCCACACCGCTGCAGGGCGGCTCGAACAGTGCCGCCGCCATCGGGCAGT CCTCCGGGGAGCTCCGGACCGGAGGGCCCGCCGCCCCCTCCTNTAGGCGCCTCC TCCCAGCCGCCCCGGGTGGCGACTCCAGCCCAGTCGTGGATTCTGGCCCTGGCCC CGCTAGCAACTTGACCTCGGTCCCAGTGCCCCACACCACCGCACTGTCGCTGCCCG CCTGCCCTGAGGAGTCCCCGCTGCTTGGTAAGGACTCGGGTCGGCCCAGTCGGAG GATTGGGACCCCCCGGATTTCCCCGACAGGGTCCCCCANACATTCCCTCAGGCTG GCTCTTCTACGACAGCCAGCCTCCTCTTCTGGATCAGAGTTTTAAATCCCANACA GAGGCTTGGGACTGGATGGGAGAGAGGTTTGCGAGGTGGGTCCCTGGGGAGTCCT GTTGGAGGCGTGGGGCCGGGACCGCACAGGGAAGTCCCGAGGCCCCTCTAGCCCCA AAACCANAGAAGGCCTTGGAGACTTCCCTGCTGTGGCCCGAGGCTNAGGAAGTTTT GGAGTTTTGGGTCTGCTTANGGCTTCNAGCAGCCTTGCACTGAGAACTTTGGTAGG GACCTCGAGTAATCCACTCCNTTTTNGGGACTGACGTGAGGCTCCCGGTGGGGAAA GANACTGACCTNTC

Sequence ID-1453SEQ ID NO: 487

 ${\tt CCGACCTGTCTCGCTCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTTTTCTGGC}$ CTGGAGGCTATCCAGCGTACTCCAAAGATTCAGGTTTACTCACGTCATCCAGCAGA TTGAAGTTGACTTACTGAAGAATGGAGAGAAATTGAAAAAGTGGAGCATTCAGAC TTGTCTTTCAGCAAGGACTGGTCTTTCTATCTCTTGTACTACACTGAATTCACCCC CACTGAAAAAGATGAGTATGCCTGCCGTGTGAACCATGTGACTTTGTCACAGCCCA AGATAGTTAAGTGGGATCGAGACATGTAAGCAGCATCATGGAGGTTTGAAGATGCC CTTATACACTTACACTTTATGCACAAAATGTAGGGTTATAATAATGTTAACATGGA CATGATCTTCTTTATAATTCTACTTTGAGTGCTGTCTCCATGTTTGATGTATCTGA GCAGGTTGCTCCACAGGTAGCTCTAGGAGGGCTGGCAACTTAGAGGTGGGGAGCAG AGAATTCTCTTATCCAACATCAACATCTTGGTCAGATTTGAACTCTTCAATCTCTT GCACTCAAAGCTTGTTAAGATAGTTAAGCGTGCATAAGTTAACTTCCAATTTACAT ACTCTGCTTAGAATTTGGGGGAAAATTTAGAAATAATTGACAGGATTATTGGAA ATTTGTTATAATGAATGAACATTTTTGTCATATAAGATTCATATTTACTTCTTAT ACA

Sequence ID 1454SEQ ID NO: 488

TAAATAGGGAATCCTTTCCCCATTGCTTGTTTTTCTCAGGTTTGTCAAAGATCAGA
TAGTTGTAGATATGCGACGTTATTTCTGAGGGCTCTGTTCTGTTCCATTGATCTAT
ATCTCTGTCACATGCACACGTATGTTTGTTGTGGCACTATTCACAGTGGCAAAGAC
TTGGAACCAACCCAAATGTCCAACAATGATAGACCGGGTTAAGAAAATGCGGCACA
TATACACCATGGAATACTATGTAGCCATAAAAAATGATGAGTTCGTGTCCTTTGTA
GGGACATGGATGAAATTGGAAATCATCATTCTCAGTAAACTATCGCAGGAACAAAA
AACCAAACACTGCATATTCTCACTCATAGGTGGGAATTGAACAGTGGGAACACATG
GACACAGGAAGGGGAACATCACACTCTGAGGACTGTTGTGGGGTGGGGGGAGGAG
GAGGGATAGCATTGGGAGATTACCTAGTGCTGGATGACGAGTTAGTGGGTGCAGC
GCACCAGCATGTCACATGTATACATATGTAACTAACCTGCACATTGTGCACATGTA
CCCTAAAACTTAAGGTAT

Sequence ID 1456SEQ ID NO: 489

Sequence ID 1460SEQ ID NO: 490

Sequence ID 1490SEQ ID NO: 491

ATGGCATCTCTCGGGACAACTGCACAAGCGCCGCAAAACCGGGGGCAAGAGAAA
GCCCTACCACAAGAAGCGGAAGTATGAGTTGGGGCGCCCAGCTGCCAACACCAAGA
TTGGCCCCCGCCGCATCCACACAGTCCGTGTGCGGGGAGGTAACAAGAAATACCGT
GCCCTGAGGTTGGACGTGGGGAATTTCTCCTGGGGCTCANAGTGTTGTACTCGTAA
AACAAGGATCATCGATGTTGTCTACAATGCATCTAATAACGAGCTGGTTCGTACCA
AGACCCTGGTGAAGAATTGCATCGTGCTCATCGACAGCACACCGTACCGACAGTGG
TACGAGTCCCACTATGCGCTGCCCCTGGGCCGCAAGAAGAGGGAGCCAAGCTGACTCC
TGAGGAAGAAGAAATCAACAAAAAACGATCTAAAAAAATTCAGAAGAAATATG
ATGAAAGGAAAAAAGAATCAGCAGTCTCCTGGAGGAGCAGTTCCAGCAG
GGCAAGCTTCTTGCGTGCATCGCTTCAAGGCCGGGACAGTGTGCCCGCA
AAGGCAAATAAATCCTTGTTTTGTCTTCACCCATGTAATAAAGGTGTTTATTGTTT
TTGTT

Sequence ID 1491SEQ ID NO: 492

Sequence ID 1492SEQ ID NO: 493

Sequence ID 1493SEQ ID NO: 494

Sequence ID 1494SEQ ID NO: 495

TTGGTACCCGGGAAATTCTTTGCCGCGTCGACGGCCGGTGAGGCAGATCACCTGAG
CCCAGGAGTTCAGGACCAGCCTGGGCAGCATACCGGGATTCCATCTNNACTAAAAA
CAGTAGGCTGGGTGTGGTGGCTCATGTCTGTAAGCTCAGGACTTTGGAAGGCCAAG
ATGGGAGGATCACTTGAGCCTGGGAGTTTGACACCAGCTTGAGCATCGTAGCCAGG
CCCTGACTCTACAAAAAAGTGAAATAATTAGCCGAGTGTGGTGGTTCACACCTGTA
ATCCCAGCTGCTCAGGAGGCTGAGGTAGGAGAATCATTTGAACCCGGGAGGTGGAG

Sequence ID 1495SEQ ID NO: 496

Sequence ID G6SEQ ID NO: 497

GGATTTTTGGTCCGCACGCTCCTGCTCCTGACTCACCGCTGTTCGCTCTCGCCGAG
GAACAAGTCGGTCAGGAAGCCCGCGCGCAACAGCCATGGCTTTTAAGGATACCGGA
AAAACACCCGTGGAGCCGGAGGTGGCAATTCACCGAATTCGAATCACCCTAACAAG
CCGCAACGTAAAATCCTTGGAAAAGGTGTGTGCTGACTTGATAAGAGGCGCAAAAG
AAAAGAATCTCAAAGTGAAAGGACCAGTTCGAATGCCTACCAAGACTTTGAGAATC
ACTACAAGAAAAACTCCTTGTGGTGAAGGTTCTAAGACGTGGGATCGTTTCCAGAT
GAGAATTCACAAGCGACTCATTGACTTGCACAGTCCTTCTGAGATTGTTAAGCAGA
TTACTTCCATCAGTATTGAGCCAGGAGTTGAGGTGGAAGTCACCATTGCAGATGCT
TAAGTCAACTATTTTAATAAATTGATGACCAGTTGTTAAAA

Sequence ID - 61SEQ ID NO: 498 nt:362

CTTATTGAAAATTTTACTAATTTCTTACTTTTTAGGTTTTAGGAGAATACTTTTGGA
TAATTGACTAGCCTCACATTATATTGATAGAGGTTCTTGAAAACTTTAATGCCAAT
TCATGTATCTTATGACTAAAATAGATAATCCATTTAGAAATTTAAGTCATTCTTGC
GTGCTTGATATGTGTCAGCACTATCCAAGTTGCTAGGGGATACAATGGTGAAGTG
AAAATATCAGCTAGGTGCCGGTGGCTCACACCTGTTATCCCAACAGTTTGGGAGG
CCAGGGTGGGAGGATCACTCAAGCACANGCGTTTCACACCAGCCTGGACAACAT
ACAAGACCCCATCTTTACCAAAAGTTAAG

CTTTATTTTTTCTGATTTTAAAAGTAATAACTAGTTTGTAGAAACATTAAAAGT

Sequence ID - 77SEQ ID NO: 499 nt: 464

GCGGCTGCTGTTGGTTGGGGGGCCGTCCCGCTCCTAAGGCAGAAGATGGTGGCCG

CAAAGAAGACGAAAAAGTCGCTGGAGTCGATCAACTCTAGGCTCCAACTCGTTAT

GAAAAGTGGGAAGTACGTCCTGGGGTACAAGCAGACTCTGAAGATGATCAGACA

AGGCAAAGCGAAATTGGTCATTCTCGCTAACAACTGCCCAGCTTTGAGGAAATCT

GAAATAGAGTACTATGCTATGTTGGCTAAAACTGGTGTCCATCACTACAGTGGCA
ATAATATTGAACTGGGCACAGCAGCATGCGGAAAATACTACAGAGTGTGCACACTGG
CTATCATTGATCCAGGTGACTCTGACATCATTAGAAGCATGCCAGAACAGACTGG
TGAAAAGTAQAACCTTTTCACCTACAAAATTTCACCTGCAAACCTTAAACCTGCAA
AATTTTCCTTTAATAAAATTTGCTTG

Abstract

Product and Method

The present invention relates to oligonucleotide probes, for use in assessing gene transcript levels in a cell, which may be used in analytical techniques, particularly diagnostic techniques and kits containing the same.